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PROBLEMS OF SPACE BIOLOGY

Volume VI

N. M. Sisakyan, Editor

"Nauka" Press, Moscow, 1967

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PROBLEMS OF SPACE BIOLOGY

Vol. VI

N. M. Sisakyan, Editor

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ANNOTATION

The collection contains three divisions. The first division treats the general problems of space biology and medicine. The second and third treat the effect on an organism of altered gravitation and the biological action of radiation.

This publication is intended for a large group of biologists, doctors, physicists, chemists and designers.

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FOREWORD

Space biology is developing successfully, both in our country and abroad. The number of problems which attract the attention of researchers is expanding continuously, and new tasks are constantly being introduced into the practice of astronautics. /3

The publication of the collections in the series "Problems of Space Biology", first conceived by Academician N.M. Sisakyan, involves a generalization of scientific data collected in many sicentific associations.

The preceding volumes have met with acclaim from the scientific community, and have been translated into foreign languages. In preparing the materials for publication, the editorial board tried to find the most adequate form for presenting the information to the reader. Thus, a logical transition was made from collections encompassing a wide range of problems to editions of narrower scope (for example, Volume V, which involved a monographic exposition of the dynamics of cerebral hemorrhage during gravitational stress).

This volume of "Problems of Space Biology" (Vol. VI) is divided into three parts.

The first involves certain general problems, and is introduced by a survey article by Academician N.M. Sisakyan, entitled "Several Problems of Ecophysiology", which he read at a UNESCO session in Paris, in 1965. This was the last public address of the late Academician N.M. Sisakyan, a prominent Soviet scientist and one of the leading figures in space biology. The other five articles in the first part develop, to a certain extent, the positions of this article, as if it were the introduction.

The principal materials of the volume encompass two problems: /4 the effect of altered gravitation on the organism, and the biological effect of radiation.

Perhaps the most significant factors related to flight into outer space are the change in the gravitational field and the ionizing radiation.

Constant attention is being given to analyses of these aspects, and some of the accumulated data is presented in this volume.

A particular feature of some articles is an examination of the combined effect of various factors of space flight on an organism. Until recently, comparatively little importance was given to the problem of combined stress, although during an actual flight the organism encounters presicely this type of effect.

Finally, mathematical research methods and approaches, based on the achievements of cybernetics, are being used more and more in the practice of space biology. These tendencies are also reflected in the materials of this volume.

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GENERAL PROBLEMS OF MEDICAL SPACE BIOLOGY

SEVERAL PROBLEMS OF ECOPHYSIOLOGY[1]

N. M. Sisakyan

ABSTRACT: The overall trends of investigations are studied in the field of ecophysiology for the period since the launching of the first artificial earth satellite. An intimate relationship is shown between space physiology and the problems of exobiology on the one hand and between space physiology and the applied problems of creating biotechnical systems and developing methods for raising the stability of the organisms on the other. Results are given for terrestrial and aeronautical studies on the effect of factors in outer space (vacuum, cosmic radiation, characteristics of the temperature regime, etc.) and flight (artificial gas environment, pressure, dynamic factors) on living organisms.

As a result of the rapid rate of development and the continuous expansion of investigations in the field of space physiology, there naturally arises a necessity of studying the results achieved and of analyzing trends in this field of knowledge. /5*

Although slightly more than 7 years have passed since the launching of the first biological satellite, our knowledge has advanced considerably. We now have available not only a tremendous amount of experimental material, obtained from experiments with animals, but also (in the literal sense of the word) invaluable information obtained during the flights of the astronauts.

In this report I have not set myself the goal of giving a general review of the materials collected, since it would be impossible in the time available to me to cite all the numerous investigations carried out in the Soviet Union alone.

---

[1] Report presented at the Second International Symposium on the Fundamental Problems of Human Existence in Outer Space. Paris, June 14-18, 1965.

* Numbers in margin indicate pagination in original foreign text.

I have therefore confined myself to examining the overall trends of investigations in the field of ecophysiology; certain specific data, borrowed from research in 1964, will be given only as illustrations of specific situations.

In rapidly developing fields of knowledge, especially those which have been conceived, so to say, on the edge of a number of scientific disciplines, problems often arise in determining the boundaries of interest and competence.

The question is far from being one of idle curiosity and I should like to pause briefly and examine it.

At the present time, ecophysiology (space physiology) can be thought of as a certain group of biological disciplines, which study characteristics of the processes of activity and behavior of living organisms of Earth when they are under the influence of the conditions of outer space or flight in rockets. /6

The complexity and the numerous problems arising in such cases have caused many ideas and methods to be proposed for solving them, not only those which definitely pertain to physiology, but also those which are of interest to the areas of biochemistry, biophysics and other aspects of biology.

As a result of this, the determination of the boundaries of competence in space physiology is of a rather arbitrary and temporary nature. The range of interest of this field of knowledge is often interwoven with the sphere of interests in exobiology, general and applied ecology, radiobiology and several other areas.

However, regardless of which specific methods of analysis are used in space physiology, no matter how far it penetrates into the adjacent fields of knowledge, its major purpose is the physiological justification of means and methods for maintaining normal activity of organisms under extreme conditions.

On the basis of a thorough study of the influence on living organisms of environmental factors and the many mechanisms of their influence, our concepts concerning physiological means for increasing the resistance of an organism have been formed; physiological recommendations have been developed for constructing diverse means for protection against the harmful effects of unfavorable environmental factors; and the ecological constants of the artificial inhabitable environment have been determined.

At the present time, the most significant of the problems of ecophysiology is that of studying the influence of factors in the external environment on living organisms.

Attention to these problems is justified by the following situations.

On the one hand, a study of the possibility of maintaining life of various living systems approximates a solution of the general biological problem of the existence of life in space, where the external conditions are extreme with respect to terrestrial forms of life. In this field, the range of interest in space physiology is intimately involved with problems of exobiology.

On the other hand, knowledge of the characteristics of the reaction of living organisms to extreme environmental factors, as well as data concerning the limits of their resistance and endurance, permit solution of practical problems concerning the creation and improvement of biotechnical systems, in conjunction with the development of means and methods for raising the resistance of the organism.

Hence, we must divide the environmental conditions underlying /7 the study into those factors that are inherent in outer space and those which are produced by the characteristics of life aboard spacecraft.

The first group includes the physical factors of outer space (vacuum, different types of space and solar radiation, characteristics of the temperature regime, etc.).

The second group includes the factors produced by the artificial environment of the space craft (pressure, gas composition of the atmosphere, temperature, etc.) and the dynamic factors associated with flight (acceleration, vibration, weightlessness, etc.).

In addition to a study of the physiological effect of each of these factors, more attention is being paid each year to studies for ascertaining the characteristics of the complex interaction (in various combinations) of these factors.

In spite of the technical difficulties involved in these experiments, their specific importance in research programs is growing constantly.

Nevertheless, it is still quite important to have actual studies of the resistance of organisms to extreme factors, including the natural space environment. The importance of this premise has been confirmed by the flight of the "Voskhod-2".

Thus, in recent times a significant number of research projects has been carried out to study the reaction of organisms and individual cells at low and superlow temperatures. The investigations in the laboratory of L. K. Lozin-Lozinskiy have shown that among the different animal phyla (the vertebrates should be excluded) there are representatives whose biological and ecological characteristics render them capable of enduring extremely low temperatures, all the way to temperatures near absolute zero. Furthermore, almost all cells, including those of vertebrates, are

potentially resistant to cooling below -80°, and even (with protective substances) to -269°. Under conditions of complete anabiosis of living systems at the temperature of liquid gases, life can apparently be conserved for an indefinite time without lowering the capacity of the entire organism or its cells. The results of the above experiments with unicellular organisms and with insects are of great significance for space biology. Apparently, low temperatures (including supercooling) can not serve as an obstacle to maintaining life for bacteria, fungi, invertebrates, and possibly even certain poikilothermic vertebrates.

Determining the limits of safe reversible cooling of living systems must occupy an even greater place in research. In this case, serious attention must be paid to study at the cellular and molecular levels, which will permit a closer approach to an understanding of the resistance of living systems to low and superlow cooling. /8

We can expect new data in this direction that is both significant and interesting.

Studies of cryolysis, radiolysis and photolysis, as well as their combined effect on the molecules of nucleoproteins, undoubtedly will provide new data for determining the effect of a number of physical agents on the resistance or destruction of living systems.

Thus, for example, M. A. Khenokh found a number of qualitative changes in albumen and desoxynucleoproteids under the influence of deep freezing and also with the complex influence of cooling and radiation (γ-rays of Co^{60} and ultraviolet radiation).

It was shown that freezing (-78°) of solutions of desoxynucleoproteids (DNP) will result in precipitation of the residue, since in the liquid phase there is increase in the characteristic viscosity, a drop in molecular weight and an increase in the asymmetry of the molecules.

The effect of γ-rays, depending on dosage, changes the molecular weight and the degree of molecular aggregation. With large dosages, molecular aggregation occurs along the longitudinal axis with the formation of rather ramified molecules. In frozen solutions, these phenomena occur more intensely. Radiation by ultraviolet produces displacements analogous to radiolysis.

Under the influence of γ-rays, at both positive and negative temperatures, a breakdown was observed in the bond between albumin and DNA. Products containing nitrogen and phosphorus were detected in the dialysate.

According to the data of A.A. Imshenetskiy et al, several enzymes undergo changes under the influence of low temperatures. By using polarography, it was shown that under these conditions the

albumin undergoes molecular rearrangement, in which it is the hydrogen bonds which basically participate. The activation energy drops most sharply with lowering of the temperature to -3°, since in such cases the lowering of the activation energy is associated with intramolecular reorganization of the enzyme (typsin).

For space physiology, it is of considerably interest to study the cooling of higher animals, especially in the light of studying the possibilities of artificial hypothermy and anabiosis. The high resistance of artificially cooled organisms to oxygen starvation is well known, as well as to several other harmful agents. This gives a basis for assuming the possible use of a similar type of biological protection relative to the emergency conditions of space flight (N.N. Sirotinin, G.D. Glod, et al.).

The data obtained indicate the capacity of animals in a state of artificial hypothermy to safely endure accelerations which are large and of long duration, the effects of ionizing radiation, and other factors (V.I. Danileyko, G.D. Glod, V.S. Oganov, N.N. Timofeyev, et al.). In a state of reversible deep cooling (body temperature +3°) white laboratory rats maintain viability after effects (acceleration, hypoxia) which are absolutely intolerable to normal animals (G.D. Glod et al.). /9

Unfortunately, at the present time the methods of safe artificial depression of reactivity for a long period of time have not been perfected; hence, research in this direction deserves worldwide consideration.

With entry into free outer space, under known conditions, we may also expect effects produced by hypothermy.

This problem must also be considered in the evaluations of physiologists, especially by taking into account the specific conditions of heat exchange at zero gravity. As far as the determination of the boundaries of endurance of high temperatures is concerned, in this field of ecophysiology we can use the huge amount of data available from other fields of physiology and professional medicine.

A second important extreme factor in outer space is the high vacuum. Research carried out recently by A.A. Imshenetskiy et al. has confirmed the high resistance of a number of microorganisms to this factor. Thus Aspergillus terreus, Micrococcus aureus and several algae (Chlorella vulgaris and others) endure a vacuum of 10^{-8} - 10^{-9} mm Hg quite well. These data have great significance for exobiology, particularly for considering problems of transspermy. However, it is well known that for more organized living substances the effect of even small degrees of vacuum has fatal consequences.

The various types of radiation are differentiated by basic biological activity.

It was assumed that ultraviolet rays in outer space are absolutely fatal to living organisms. However, there are many factors which oppose this view. In particular, we may mention photoreactivation, or screening the effects of various chemical materials included in the composition of the cells and their membranes (for example, pigments), which are capable of increasing the overall resistance to ultraviolet of the cytoplasm and the nucleus. It is quite probable that the harmful effect of ultraviolet radiation on terrestrial organisms is due first of all to the fact that under terrestrial conditions the organisms have not adapted to it or perhaps have lost their resistance in the process of evolution. It is interesting that the enzyme of photoreactivation may be used only when irradiating cells with rays that have not reached the surface of the Earth. At the same time, ionizing radiation lowers the effect of photoreactivation.

Cytological studies of the effects of short-wave ultraviolet /10
radiation are of even more interest for space physiology. Physiological, cytochemical and morphological changes in certain infusoria may be sensitive indicators of the biological effect of ultraviolet radiation and thus serve as unique dosimeters.

For space physiology dealing with long-term flights, certain practical significance will be found in the problem of "ultraviolet starvation", determining the necessary level of radiation of the crew of the spacecraft.

On the other hand, the equipment designed for astronauts outside the space craft must naturally provide protection against harmful effects from ultraviolet radiation. In such case, however, numerous problems arise which are associated with the selection of suitable materials used for constructing such equipment.

Incomparably more serious is the danger of ionizing radiation. However, this special problem, pertaining to the area of radiobiology, will not be discussed here, although in a number of its important aspects it is intimately associated with problems of space physiology. This is especially true for the study of the combined effect on an organism of a number of factors including radiation.

A good model for such investigations is the more or less complete artificial simulation under laboratory conditions of outer space as well as conditions on any other planets.

In this respect, I must briefly mention the research being carried out on modeling the Martian climate.

An experimental chamber has imulated the conditions on Mars, based on gas composition of the atmosphere, pressure, temperature and ultraviolet radiation. It has been shown that of these factors, it is only the ultraviolet radiation which has limited the life capac-

ity of microorganisms. The greatest resistance was that of bacteria which form spores and pigment microorganisms. In particular, fungi (which form a black pigment) did not perish at a UV radiation dosage equal to $4.04 \cdot 10^8$ erg/cm^2, which again demonstrates the protective role of pigment (A.I. Zhukova et al.).

In the above-mentioned studies it was shown that not only do very thin layers of soil give protection from the bactericidal effect of ultraviolet radiation, but the cells of the microbes themselves provide protection. Thus, for example, a screen of one layer of cells (1.9 μ in diameter) reduces the bactericidal effect of the rays by a factor of 4.

In passing, let me mention that in the laboratory of Lozinskiy, the cycle of development of terrestrial infusoria was also studied under conditions approximating those of Mars. Here it was shown that these infusoria can adapt to the conditions of /11
diurnal change in temperature observed on Mars and to a periodic drying and freezing to -78°. This unicellular animal imitates well an organism which could exist under conditions of Martian soil or in a plant layer from the surface of this planet. Such a resistance on the part of infusoria is apparently due to their high resistance to cold as a result of their ability to endure loss of water.

The examples cited give some idea of the astonishing adaptivities of different members of the terrestrial organic world.

Discovery of the intimate mechanisms of the adaptation of living substances to the extreme conditions of space opens the way to increasing their resistance and to the possible means of constructing protective measures.

Now let us return to the physiological evaluation of the role of the dynamic factors of flight, which from the viewpoint of the current state of development of astronautics, may possibly have even greater significance that the factors analyzed above.

A huge amount of research, including the fundamental and long-term studies of many authors, has been devoted to physiological analysis and to determining the boundaries of endurance of acceleration.

With respect to the practical requirements of astronautics, primary attention has been paid to the problem of transverse stress, that of the transition from excess weight to weightlessness, and also to the problem of weightlessness itself. This branch of space physiology is being rapidly developed at the present time.

It is not feasible to list even the most essential achievements in this field. For now, let us restrict ourselves to unclear and poorly developed problems.

The investigations undertaken by Ya. A. Vinikov, V. G. Yeliseyev, et al., using electron-microscopic and histochemical methods have permitted a new look at the change in the structure and functions of cells of various organisms and tissues in response to the effect of acceleration.

It is still too early to give any results from these investigations. However, the impression is growing that here we shall encounter a rather complex pathogenetic mechanism of cellular injury. This injury apparently is not always evident in the dynamics of external indications of the physiological functions, whereas subsequent damage to the enzyme systems, changes in the metabolism and even injury to the cellular structure can be very distinctly observed.

It seems to me that in the field of physiology of acceleration, besides the attention it deserves and the appropriate study of the general mechanisms of regulating the functions, it is even more important to study the processes which occur at the cellular and subcellular levels.

In this respect I wish to mention that earlier, in studying /12
the effect of space flight on the nuclei of cells in the bone marrow and spleen of mice, N.P. Dubinin, M.A. Arsen'yeva et al discovered the occurrence of certain peculiar injuries to the nuclei of the cells, in the form of adhesion of chromosomes and a slight increase in the frequency of mutations.

The studies then carried out under terrestrial conditions indicated that vibrations (35-70 Hz, 60 min) influence the mitotic activity of the cells and produce disorders, similar to those which were observed after space flight.

Experiments on mice in studying the effect of accelerations, carried out in a centrifuge with acceleration from 8 to 20 g, showed that this physical factor exerts an influence on the nucleus of the cell similar to that of vibrations.

Analogous phenomena were observed in experiments during free flight of an aircraft along the Kepler parabola, with combined effects of vibration, acceleration and weightlessness. The inclusion in the experiment of a factor such as the condition of weightlessness, resulted in a real increase in the frequency of fragmentation and (we might also assume) to a non-division of the chromosomes as well.

Thus, a study of the effect of the dynamic factors of flight, including their effects from radiation, showed that the effect of these factors will result in disorders in cell division.

We may assume that the change in the normal process of division under the conditions described is accomplished both indirectly

through hormonal and immunal changes in the organism and possibly as a result of a direct physical effect of the above factors on the apparatus of the cell, (adhesion of the chromosomes at different stages of the cellular cycle, displacement of the chromosomes and their expulsion from the spindle). Obviously the basis of these phenomena is the suppression of the process which develops division of the cell, and also disorder in the function of the apparatus of division.

The long-term effect of the different factors producing disorder in the metabolism of the cell may lead to an elongation of the cell cycle and to the suppression of the synthesis of desoxyribonucleic acid and to the appearance of different restructuring of the chromosomes. Analysis of the sensitivity of individual phases of the cellular cycle in the bone marrow, in view of the influence on mice of vibration and rotation in a centrifuge, showed that it is the stages of presynthesis and synthesis of dexoxyribonucleic acid that are most sensitive to these effects.

Study of the protective substances produced by the unfavorable effects of vibrations showed that several of them, for example serotonin, protect the cells of the bone marrow from such disorders as adhesion of the chromosomes.

Here we may list several of the insufficiently studied facts which characterize change at the cellular and sub-cellular levels, arising as a result of the effect on the organism of the dynamic factors of flight. /13

At the present time it is difficult to evaluate completely the significance of these displacements for the functional state of an organism.

As I have already mentioned, in such cases we have not observed any notable change in the physiological functions, changes in the basic clinical constants of the peripheral blood, or disorders in behavior or working capacity.

Consequently, we have as yet no basis for re-evaluating the significance of these facts or for interpreting them with any misgiving.

Along with this, I consider it essential to emphasize once more that the facts which have been discovered must be taken into account in a further careful study, especially with respect to the problem of long-term flights. They also substantially augment the picture of overall changes, in which there are still many gaps.

Thus, at the present time the functions of the nervous system have yet to be adequately investigated with respect to the effect of acceleration on an organism. Apparently we are correct in expecting to obtain important data by setting up detailed electrophysiological investigations which take into account the hemodynamic

displacements that are possible as a result of acceleration.

As the interesting studies of Yu. Ye. Moskalenko et al. have emphasized, the high intensity of the cerebral blood flow and the peculiarities of the anatomical structure of the vascular system of the intracranial cavity would give reason to assume that one of the reasons for the restructuring that occurs in the organism of man and animals under the influence of gravitational forces is the disturbance of the blood supply from the brain.

Data obtained in experiments on man and animals show both a high sensitivity of the system of the intercranial blood circulation to redistribution of the blood in an organism under the influence of gravitational forces, and the high compensatory possibilities which are capable of assuring a satisfactory blood supply to the central nervous system within broad limits of gravitational forces; these limits may be notably expanded by proper training and possibly by the use of certain pharmacological preparations.

Here we again see that the degree to which the effective mechanisms of individual factors can be explained indicates the possibility of influencing the course of events in the manner desired. In the respect I would like to cite the experiments of P.V. Vasil'yev et al., which showed that the sensitivity of animals to a number of pharmacological preparations (glucosides, sympathomimetic remedies, narcotics) has been found to be notably changed in the period after the effect of accelerations.

These data permit us to use therapeutic remedies more rationally and also help us to better understand the pathogenesis of the disorders observed under the effects of acceleration.

Among the problems of space physiology, a special place is occupied since the very beginning by the study of weightlessness. /14

The problems of duplicating weightlessness under terrestrial conditions have made experiments on spacecraft the major reason in studying this problem. The successful flights of the astronauts and in particular the 5-day flight of V. Bykovskiy as well as the brilliant performance of A. Leonov during his walk in space have quite rightly produced a feeling of satisfaction and optimism.

Along with this a thorough and detailed survey of the level of our contemporary knowledge requires very intense and serious attention to this problem.

In addition to the study of the peculiarities of the functioning of the system of analyzers, hemodynamics, and metabolism, our attention must be directed in two other directions as well.

First, there is the study of the endurance of an organism toward acceleration after previous subjection to a state of weight-

lessness; secondly, there is the investigation of the physiological effect of long-term weightlessness.

Of familiar interest in this respect are the statements of P.A. Korzhuyev. In studying the change in the synthesis of hemoglobin in the phylogenesis of the animal world, the peculiarities arising when animals leave the water and come onto dry land, the author came to the conclusion that the evolution of this function represents an experiment, carried out by nature over a period of millions of years, an experiment which may give certain indirect data for posing and solving one of the problems of weightlessness.

In this case, the author starts from the premise that the habitation of animals in a water environment, unlike life on dry land, in some ways duplicates the conditions of weightlessness.

Based on the facts of the appearance of bone marrow in land vertebrates and its progressive development in higher orders of land mammals, as contrasted to its reduction in water mammals, which have adapted to the conditions of the water environment, the authors assumes that long-term weightlessness may be expressed extremely unfavorably in hemopoiesis.

I should also like to recallthe idea of K.E. Tsiolkovskiy (1882) as to the possibility of substantial changes in the development of organisms under conditions of weightlessness. It has not lost its applicability even now and we apparently cannot exclude the probability that for space stations which are inhabited for some period of time or during lengthy interplanetary flights of space ships, there will arise the necessity of artificial gravitation and the establishment of optimal regimes which will support this explanation in the very near future.

We should also consider other precautions which will guard against the possible onset of undesirable consequences from lengthy weightlessness.

In this case, we are concerned with a special selection and /15
training of astronauts, the construction of a preventative regime of work and rest on the craft, etc.

A recent experiment on the "Voskhod-2" also showed the exceptional significance of a detailed analysis of the problem of biochemistry with respect to solving future problems of astronautics, associated with the establishment of space objectives and the carrying out of different tasks outside the craft by astronauts.

Several achievements in the field of space physiology facilitate a rational and practical solution to the problems of guaranteeing life during lengthy space flights. In this plan, the most important spot is occupied by the physiological studies, which determine the means for creating an artificial environment inside the cabin of the spacecraft.

In this case, it is important to determine the limits of permissible fluctuations of the environmental parameters such as barometric pressure, gas composition, humidity and temperature. These questions have been successfully treated for some period of time in intimate relationship with the progress of space apparatus. In recent times, considerable attention has been given to the choice of components of the gas environment of the airtight cabin. Though acceptable solutions have already been found for short-term flights and several of them have been tested, this problem still remains unclear in many respects for long-term flights.

Of unquestionable interest are the attempts to include helium in the composition of the artificial atmosphere. Among the numerous works devoted to the study of this problem, let us note the studies of A.G. Zhironkin et al., which experimentally established the maximum allowable safe concentrations of oxygen with a mixture of helium, with respect to various animal species. Besides this, the authors obtained a number of hopeful experimental data, pertaining to the long-term effects of helium on an organism. In particular, it was established that in long-term experiments both animals and people prefer to breath a helium-oxygen mixture rather than a nitrogen-oxygen mixture because of the physical properties of helium, which facilitates reducing the resistance to breathing and increasing alveolar ventilation.

V.V. Boriskin et al. examined the possibility of survival for long periods of time in a helium-oxygen atmosphere, using biological material at various organizational levels.

Thus, a study of the growth of frog eggs and chicken embryos did not reveal any differences between the time or nature of embryogenesis of the yound, whether they were incubated in helium-oxygen or nitrogen-oxygen media.

The studies of A.G. Dianov, A. G. Kuznetsov, et al. are of practical importance; these investigators demonstrated the possibility of prolonged survival of man (10 to 25 days) in a helium-oxygen atmosphere.

No changes in the basic physiological functions of the subjects were found, with the exception of a change in voice. /16

According to the data of Yu. V. Krylov, for example, breathing a mixture of helium and oxygen shifts the sound spectrum of the voice toward the higher frequencies by about 0.7 octave. The decrease in intelligibility does not exceed the permissible level.

Studies in this regard should be continued, and steps should be taken in particular to explain the biological significance of other inert gases, as was urgently proposed in his time by L. A. Orbeli.

In accordance with the natural effort of designers to build cabins with reduced pressure inside them, studies are in progress to investigate the possibility of prolonged existence of organisms under these conditions.

Thus, in the experiments of D.I. Ivanov, V. B. Malkin et al., it was shown that it is possible for man to survive for a long time (up to 30 days) under conditions of reduced barometric pressure, corresponding to elevations of 3000, 5000, and 7000 meters, maintaining the normal partial pressure of oxygen by enriching the cabin atmosphere with it.

The authors did not observe any significant disturbance of functions which could have been related to the reduced barometric pressure or the increased oxygen content.

The results of these and many other experiments are surely encouraging. It seems to me, however, that a great deal of difficult work still lies ahead.

High vacuum levels involve the danger of decompression changes and an increase in the concentration of oxygen, coupled with a manifestation of its toxic effect.

Clearly, all of this will make it possible to form an acceptable atmosphere for the cabin under normal flight conditions, but it will be difficult to maintain when emergencies arise.

Particularly difficult and specific problems arise for ecophysiology in connection with the construction of artificial ecological systems, when the individual components are various animals and plants.

The characteristics of the growth of biomasses, the production of oxygen and the absorption of carbon dioxide, and resistance to the effect of hostile factors are only a few of the problems that require physiological specialists who work in the field of constructing ecosystems.

As A. B. Rubin et al. pointed out, a description of the life processes in an ecological system requires new approaches to the determination and study of the state of their resistance and reliability, which is possible only by applying modern mathematical and thermodynamic methods of analysis. /17

The field of space physiology includes the study of the problem of physiological rhythms, applicable to the conditions of long flights, a basis for rational work regimes and rest periods for the crew, as well as many other problems deserving of attention.

During long flights in space, the astronauts may be subject to the influence of various hostile factors. This makes it nec-

essary, when preparing for such a flight, to try to build up the adaptational reserves of the organism as much as possible.

This can be accomplished in principle by two methods which are by no means mutually exclusive. The first is the use of various training programs, which naturally increase the adaptational reserves of the organism. The second is the use of pharmacological and biologically active agents.

In view of the fact that under flight conditions the organism is simultaneously subject to the influence of many factors, the idea naturally arises as to the expediency of using training methods to increase resistance which cover a very broad spectrum of nonspecific effects. It must be kept in mind,however, that in a system of methods which increase the adaptational reserves of an organism, there must also be those which develop specific protective mechanisms for the most important flight factors.

I should like to illustrate this statement with the following example. Resistance to sudden acceleration can be increased by nonspecific training methods, by physical exercises for example, or by active acclimatization in the mountains and the like. At the same time, the resultant disruption of voluntary actions, respiration and speech under the influence of stresses can be overcome in the course of training in a centrifuge, thus developing in the subjects the proper motor pathways and rendering respiration and speech effective under these conditions.

Attempts to find rational systems for training astronauts have naturally devoted attention to studies in the mountains. However, it should be taken into account beforehand that acclimation to the conditions in high mountain regions, especially in conjunction with muscle stress, is one of the most effective ways of solving this problem.

As a matter of fact, recent studies in the Caucasus and in Tyan-Shan have shown that subjects, after a rather long "stepwise adaptation" to altitudes of 2000 and 4000 meters, with occasional excursions to greater heights, showed a significant increase in their resistance to transverse stress (1.5 to 2 g) and to severe hypoxia.

Adaptation is an extremely complicated process. It involves /18
literally all regulation levels, and almost all physiological systems of the organism are affected.

This is obviously the reason why, regardless of the long period of time spent on this problem, our knowledge is still far from complete and many scientists are conducting further tests.

One of these efforts has involved the experiments of N. N. Sirotinin, Z. I. Barbasheva, V.B. Malkin et al., who have shown

that animals (white rats) from which the cerebral cortex, pituitary, adrenal glands and thyroid gland were removed separately, adapted to conditions of hypoxia. However, the adaptation mechanisms often worked in unusual ways. For example, after the pituitary was removed, animals which lived for a long period of time under high-altitude conditions did not show the characteristic reaction of erythropoiesis, but their resistance to sever hypoxia did increase somewhat.

An extremely promising field, in my opinion, is the study of the processes of adaptation on the cellular and subcellular levels. We can expect considerable progress in this field, especially with the use of modern methods of studying tissue respiration.

Hence, the materials presently available indicate that a controlled change in resistance is possible for any organism, beginning with man and ending with plant cells. The means for changing the resistance of highly diverse animals are essentially unique. They include repeated action of an agent which is directed (in the final analysis) at cellular metabolism and evokes adaptive changes in the cell chemistry. Among such agents we can include hypoxia, muscle exercise, temperature changes in the ambient medium, and several pharmacological preparations. To be sure, a single application of some factor can also increase the resistance of an organism. Thus, for example, a single application of severe hypoxia or the performance of intense muscular exercise causes changes in the oxidation metabolism of the cells, which is accompanied in the case of intense muscular exercise by increased consumption of energy-producing substances, an adaptive increase in the activity of the oxidizing-reducing enzymes, an increase in the anaerobic liberation of energy, and (in conjunction with the latter) accumulation of non-oxidized metabolic products and an increase in the oxygen debt. During the adjustment period, there is an excessive accumulation of energy sources (glycogen, phosphocreatin), protein enzymes, and various biologically active substances (myoglobin, glutathione, ascorbic acid, creatin, etc).

These processes are observed in various tissues of the organism. These reactions disappear if there is no repeated occurrence of /19
the same stressors. When the latter do recur, there is another set of changes in the biochemical processes in the cells, followed by the development of an adjustment phase. The main feature of the latter is that the adaptive processes are completed, become more economical, are summed and fixed, i.e., they remain as an after-effect for long periods of time. The result is what we call adaptation. The cells "learn", as it were, to react more economically and "expediently" to the action of stressors, and the resistance of the cell structures increases.

It should be pointed out that changes in the cell chemistry are not limited only to changes in the nature and rate of the metabolic processes. Obviously there are some other, still insuf-

ficiently understood processes (as far as their mechanisms are concerned), which lead to an increase in the resistance of cell structures in response to the action of agents of highly diverse kinds, which affect not only the metabolic processes but also act directly on the structure of the cell itself.

Thus, for example, it was found that muscle tissue and the tissue of the cerebral cortex, in rats adapted to hypoxia, become resistant to the action of ethyl alcohol or high concentrations of caffein; the absorptive properties of the reticuloepithelial tissue for vital stains decrease; there is an increase in the osmotic resistance of the erythrocytes. An idea of the structural changes in muscle tissue can also be gained by measuring the electrical conductivity and dielectric permeability of the muscles in vivo. The properties of the structural and contracting proteins of the skeletal muscles change in a certain way; it is found that in rats adapted to hypoxia, the rate at which the actomyosin complex is formed (after dissociation of this complex under the influence of ATP) is greater than in control animals (Z. I. Barbashova).

Since the repeated action of diverse stressors on the organism can produce a number of additional changes in the cell chemistry, it becomes understandable why training for hypoxia (for example) increases the resistance of the organism to the effects of acceleration, radiation, cooling, or performing intense muscular exercise.

Experimental data indicate that changes in cell chemistry under the influence of extreme factors is noted at all levels of organization of living creatures. The production of adaptation, with the repeated action of stressors, is accompanied by an increase in the nonspecific resistance of the organism. Consequently, we have a sufficient basis for stating that the adaptive changes on the cellular level are the cause of the nonspecific resistance of the organism.

Adoption of this point of view makes it necessary to carry /20
out further studies and to devise nonspecific methods for increasing the resistance of the organism to extreme factors, but of course specific training methods must be employed as well.

With regard to the latter, special attention has been devoted to methods intended to supplement the neuromuscular mechanisms of regulating physiological functions, as well as the formation and adoption of professional methods which are required for the astronaut to perform tasks, scientific research projects, and other operations.

For investigations of this kind, extremely valuable materials are provided by observations made directly under actual conditions of space flight.

Each flight of this kind is a new and important step in the conquest and exploration of the universe, and each such flight

directs our attention to new problems of space physiology.

Of particular importance from the standpoint of the physiological results obtained was the 5-day flight of V. Bykovskiy on board the "Vostok 5", as well as the flight of the astronauts P. Belyayev and A. Leonov on board the "Voskhod 2", when a man took a walk in space.

Not counting the operations involved in locking, a definite program was carried out during the flight of the "Voskhod 2": the temperature was about +18°, the humidity 35-40%, and the pressure was the normal value found on Earth.

The crew landed the spacecraft by using a manual control system. In the flight described, as well as in previous ones, there were no changes noted in the health of the crew, even in the thorough post-flight examination.

Of course, it is particularly interesting to study the working ability and biomechanical features of motion when the astronaut is moving about freely outside the spacecraft.

Astronaut A. Leonov gives the following report on some of these features:

"It is impossible to stop turning, no matter what movements one makes; I knew this, having become practically acquainted with it in my pre-flight training, so that I felt that the only way I could slow down my movement was by twisting the umbilical. And, in fact, my angular velocity gradually decreased. It is true that by grasping the umbilical I could even have created a moment which would have stopped the motion of my body around its transverse axis, but I did not want to do this. It made it possible to make more observations and there was no need to waste time.

After a while I pulled myself back to the ship by yanking on the umbilical rather hard, and had to use my hands to fend off the the spacecraft, which began to approach me rapidly. I thought first of all about not striking the window on my space-suit against the ship. However, as I reached the airlock, I broke the force with my hands. This was very easy to do, and I am sure that once /21
having adapted, one can move about quite smoothly and in a coordinated manner under these unusual conditions. I felt very elated and cheerful, and did not want to come back inside from open space; I again pushed myself away from the door of the airlock to see how I acquired my angular velocities during the first moment after the push. I found that the slightest change in direction of application of force led to rotation in the corresponding plane. Obviously people who will be working in space will have to spend a while getting accustomed to a state of weightlessness. As far as the so-called "psychological barrier" is concerned, which is supposed to be an insurmountable barrier to a man preparing to

meet the depths of space face to face, I neither felt any such barrier nor thought there could be one.

I put away the camera with which I had recorded my walk in space on film, and tried to re-enter the airlock, but this did not prove to be so easy. Movement inside an inflated space-suit is somewhat limited. Quite a bit of strenous physical effort was required, and my farewell to the cosmos was prolonged somewhat. Finally I got into the airlock, and after a short time was in the cabin once again with Pavel Ivanovich, who congratulated me on my successful completion of the program for the walk in space. Despite the rather intense physical effort required, the independent life-sustaining system appeared completely intact, and I did not suffer any lack of air nor any unpleasant temperature variation. However, when I sat down in my seat, I felt the sweat running down my forehead and cheeks. I think that it is time for some of those journalists who sat that space is a good place for a pleasant stroll, to try it themselves."

A few years ago the very first pages of space physiology were written.

Now we have accumulated quite a volume of material and I think we can proceed to sort it out into separate chapters.

Our goal is that designers, astronauts, and scientists should find in these papers, that which interests them and is necessary for the progress of astronautics.

THE PHYSIOLOGICAL EFFECTS OF GRAVITATION

O.G. Gazenko and A.A. Gyurdzhian†

ABSTRACT: Several general questions on the biological role of gravitation and also the physiological effects of weightlessness observed in biological experiments and in astronauts' flights are discussed. The mechanisms of adaptation of an organism to new gravitational conditions, the role of separate parts of the nervous system, and compensations and replacements of functions in the following spheres are examined: sphere of afferentation and analyzer activity; effector sphere and coordination of movements; sphere of regulation of the vegetative functions. Several conclusions are drawn on the ways in which studies should be made on the methods for selecting, preparing and conditioning the astronauts for unusual conditions in future lengthy flights.

Back in 1823, in the poem "Don Juan", Byron wrote: /22

> " ... for we must deem the mode
> In which Sir Isaac Newton could disclose
> Through the then unpaved stars the turnpike road,
> A thing to counterbalance human woes;
> For, ever since immortal man hath glow'd
> With all kinds of mechanics, and full soon
> Steam engines will conduct him to the moon."

Remarkable words, remarkable foresight....

In recent years, mankind has succeeded in doing very much in this direction, has succeeded in achieving outstanding results. But at the same time, there continue to be many complex problems involved in our journey into space. From among these problems, we would like to make note of, and to discuss in this paper, the problem of the physiological effects of gravitation.

The study of the physiological effect of weightlessness is a new and exceptionally important problem for manned space flights. It is very interesting for theoretical physiology as well. The

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fact is that the state of weightlessness is a remarkable experimental condition for studying the general rules of the analyzer function of the central nervous system, and thus the behavior and reactions of an organism under changing conditions in the environmental medium.

However, we are deeply convinced that the physiological effects of gravitation can be evaluated correctly only by understanding its significance in a general biological sense, in the individual and evolutionary development of organisms as one of the moving forces of evolution and ecological constants of the Earth. In this case we must remember that living organisms, in the process of evolution, encountered only a relatively short-lived effect of inertial forces (accelerations) which were either added to the gravitation force or were subtracted from it (jumps, falls, etc.). This was essentially the effect of impact accelerations.

Only the technology of the 20th century, connected with the achievement of high speeds of motion, provides for putting living organisms under conditions of prolonged acceleration effects or under conditions of reduced gravity and weightlessness. The prospects of flights to different celestial bodies, whose mass is greater or smaller than that of the Earth, produce the possibilities of entering into other gravitational conditions, into conditions of increased or decreased gravitation.

In our opinion, the fact that living organisms in the course /23
of evolution did not encounter a prolonged effect from changing gravitational and inertial conditions, must have made an impression on the characteristics of the reaction of the organism. We can assume that the organism does not have any ready-made specific mechanism for adapting to the effect of this factor, ready-made mechanisms for compensation and representation of the functions which are damaging in this case (and in the same way, to the effect of large doses of ionizing radiation which living creatures, as a rule, did not encounter in the past). This circumstance should be considered in analyzing the reactions of an organism to changing gravitational conditions, in examining the question on the possibility of conditioning it for prolonged and repeated action of accelerations and generally changing gravitational conditions.

Obviously, we must make some stipulations here. We made reference to the effect of gravitational, as well as inertial, forces, i.e. accelerations.

As far as we know at present, these forces in biological effect are mutually equivalent.

We will not examine in this paper the biological effect of those dynamic factors of flight which are relatively short-lived effects of acceleration and vibration. We will be mainly interested in the reaction of an organism to a prolonged exposure to

weightlessness.

In fundamental studies by Vander, Vrabiescu et al and in a number of other works [13, 48, 59, 60, and many others as well], it has been shown that the growth of animals under the prolonged effect of acceleration shows an outstanding effect on the formo-genesis, the formation of vegetative and animal functions, on the reactivity of animals in relation to various accelerations. These works show that gravitational conditions are not insensitive to biological relationships, but, on the contrary, play a very significant role.

There is also great interest in this question: which mutual relationships are affected by an increase and decrease in gravitation or weightlessness; how validly and with what corrections can the results of experiments with prolonged accelerations be extrapolated for states of weightlessness. It is very tempting to try to construct a single theory on the effect of acceleration and weightlessness on an organism as physical factors of one category - gravitation [16]. This question can probably be answered after corresponding biological experiments in space flights and a comparison of their results with analogous studies in laboratories.

In connection with the physiological effects of weightlessness, we have, unfortunately, limited materials which were obtained under the following experimental conditions:

1. Manned space flights in Soviet and American spacecraft /24 (lasting up to 5 days).

2. The flights of animals and other biological subjects in high-altitude rockets, artificial Earth satellites, and spacecraft.

3. Experiments with short-lived weightlessness produced in aircraft and in special test units as well: elevators, towers, etc.

4. Studies accomplished with the aid of processes which modeled certain kinds of weightlessness effects (immersion into water, hypodynamic conditions, etc.).

The results of the latest Soviet manned space flights in "Voskhod" and "Voskhod-2" are a great contribution to the study of the problem of the physiology of weightlessness. In this respect, the data obtained by A. Leonov's walk in space are particularly important. We deem it opportune to try to give a brief survey of the data and an analysis of some of the materials on the physiology of weightlessness obtained up to the present time.

In understanding the physiological effects of weightlessness, we can note a certain evolution of opinions. Not long ago, before the first direct experiments in space, particular attention was paid to a possible adverse direct effect of weightlessness, as a physical (mechanical) factor, on the basic physiological functions

of an organism: circulation, respiration, intake of food and water, digestion, and other processes. These ideas were derived, in particular, from the basic laws of hydrostatics and hydrodynamics [49, 51, 52]. However, as the first biological experiments on high-altitude rockets, artificial satellites, and space ships showed, the stresses caused by the direct action of weightlessness on the corresponding systems were minimal and rather easily neutralized by the multiple mechanisms of adaptation and compensation [24, 25, 35, 56, 57].

Subsequently, in analyzing the possible physiological effects of weightlessness (and also of accelerations), the researchers began to pay more attention to the reflex mechanisms, and to the interaction among separate sense organs as well.

In this plan, concentrated studies were conducted on the dynamics of regulating the circulatory system during the effect of acceleration, decreased gravity, and also under conditions which imitated different effects of weightlessness (immersion into water, adynamic conditions, etc.).

Many authors have explained the interrelationship among the different sense organs (analyzers) relative to the state of weightlessness. Valuable information was obtained, for example, on the interrelationships of the optical, vestibular, and proprioceptive analyzers [14, 45, 56, et.al.].

Particular attention was paid to the state of sensitivity of /25
the vestibular analyzer. Some researchers stated that, in the state of weightlessness, according to the well-known assumption by Weber and Fechner, its sensitivity will increase sharply. In this case, as a result of the interaction among separate parts of the vestibular apparatus (the otoliths, semicircular canals), according to this point of view we can expect that even small accelerations will affect the sharp sensory and motor reaction in the state of weightlessness [33, 34, 53, 56, et.al.]. On the other hand, other researchers stated that the vestibular sensitivity in the state of weightlessness will remain stable or even decrease. Studies on man, carried out by creating a state of weightlessness in aircraft, led to such a conclusion [29, 39]. It is true that the brevity of the state of weightlessness and the alternating effect of acceleration and weightlessness in these experiments limit the significance of the results obtained.

Formulation of this question has understandably great significance for solving the astronauts' practical problems connected with the development of systems of artificial gravitation [17, 57] by preventitive and conditioning methods.

Unfortunately, the results obtained from the space flights still do not ensure a complete answer to this question.

On one hand, the cosmonauts (G. Titov and B. Yegorov) observed that abrupt movements of the head and opto-kinetic irritations aggravated the general condition and coincided with separate vestibular-vegetative disturbances without a noticeable nystagmus reaction (according to Yegorov).

On the other hand, the cosmonauts on "Voskhod" and "Voskhod-2" noticed that their general condition and efficiency did not seem to relate to the stabilization or rotation of the craft around its axis (up to one revolution 20-40 sec). The cosmonaut Leonov also had no vegetative disturbances in connection with the vestibular and opto-kinetic irritations while he was outside the craft and while his body rotated in different planes with a fairly high angular velocity. Moreover, studies on the electrical sensitivity of the vestibular apparatus (to a galvanic current) conducted on board "Voskhod" would also seem to indicate that the vestibular sensitivity is not increased in the state of weightlessness. However, we were speaking in this case of the sensitivity to electrical irritation, and not to adequate irritation, and we are inclined to consider that this question requires further study.

It is unquestionable that, in order to analyze and understand the complex and multiform picture of the physiological effect of weightlessness, we must start from a concept of the reaction of an organism as a single entity. In this case, we must consider its individual characteristics and all previous experience in life. In /26
this respect, the synthetic principle founded by I.P. Pavlov can serve as such an "Ariadne's thread", which ensures finding the right path in the labyrinth of the most complicated interrelationships of an organism and the environment.

Guided by these assumptions, let us attempt to examine the physiological effects of weightlessness in the following aspects:

- Sphere of afferentation and analyzer activity;
- Effector sphere, coordination of movements;
- Sphere of regulation of the vegetative functions.

SPHERE OF AFFERENTATION AND ANALYZER ACTIVITY

It is well known that a spatial analysis is carried out by the complex integrated activity of a whole complex of analyzers; vestibular, optical, auditory, impulse, skin, interceptive, and others.

We would like to note here that the relative role of different analyzers differs in relation to the level of evolutionary development of the organism, the ecological conditions of its habitat, and its previous life experience [31]. In relation to these conditions, one or another analyzer plays an important role in the activity of

a living organism. The academician L.A. Orbeli emphasized the significance of so-called leading afferentation in the behavior of animals [10, 23].

The second condition which deserves particular examination involves the exceptional role played by the impulse analyzer. I.M. Sechenov said that the impulse analyzer and muscular sense are the basis on which all our afferentation, and all our sensing of the outer world, are formed [30]. In recent years, E.Sh. Ayrapet'yants has emphasized the important role of the impulse analyzer in spatial analysis. It is true that I.S. Beritashvili is of another opinion. He maintains that, on the contrary, the vestibular analyzer plays the most important role in spatial orientation [3, 4, 8].

The vast possibilities of compensation and representation of analyzers which are dying out is of particular interest in the mechanism of spatial analysis. This phenomenon of substitution of the role of some analyzers by others in spatial analysis is by no means instantaneous, but is a complicated process which requires definite time and conditioning. For example, if the removal of both of the eyes of an animal prevents him from making a conditioned-reflex jump, then by gradual removal of the two eyes, this coordinated act is preserved, i.e. the impulse analyzer gradually takes on the functions which were formerly carried out by the sight [6, 7].

In this light, it becomes understandable how, for example, in /27
the process of training a pilot for blind flights, the sight takes on the leading afferentation. The great diversity of subjective reactions (sensations) to the state of weightlessness also becomes understandable [12, 13, 38, 40].

Some astronauts did not experience any illusions on the irregular position of the body in space, and they detected the approach of weightlessness because the subjects were "swimming" and because of a "light-weight feeling". Others, at the very first moment of the transition from accelerations into weightlessness in a short space of time had illusory sensations of an incorrect position of the body in space ("head over heels"). In a number of cases (K. Feoktistov and B. Yegorov), the illusions regarding the position of the body in space occurred after some time and lasted with opened and closed eyes [3, 24, 25].

The astronauts who noticed similar illusions did not consider them to be extremely unpleasant and unbearable. They described them as having a certain discomfort.

The data regarding the good orientation in space of the cosmonauts on "Voskhod-2", particularly Leonov during his walk in outer space are of immense importance.

The "top-to-bottom" sensation in the cabin was limited by its interior, and even during rotation of the craft relative to the

plane of the orbit ("torsions"), the astronauts did not notice any sensation of reversed position.

The conditionality of concepts of "top-to-bottom", as well as the practical necessity of being accurately oriented in space outside the craft, required selecting a system of coordinates which would take its longitudinal axis and the position of the Sun into consideration. Orientation was also simplified by the fact that a movie camera was placed on the "top" of the air lock. When inside the air lock, the problem of orientation became more complicated, but Leonov did not notice any disagreeable sensations.

After leaving the craft, the astronaut used the system of coordinates according to the scheme described. However, if the craft did not fall within the field of vision, the orientation was destroyed, and it was not easy to determine rapidly the probable location of the craft. On the whole, we have the impression that Leonov, under these conditions, evaluated the situation adequately and, despite the exceptional novelty and irregularity of the situation, did not experience any serious nervous-emotional stress.

All this indicates the outstanding importance for an astronaut to have previously selected visual reference points for orientation in space and to have developed the necessary skills preliminarily. It seems to us that this condition emphasizes the great possibilities for rebuilding and conditioning mechanisms for analysis in space. The visual information on the distribution of objects /28
in space in this case seems to suppress the uncommon vestibular signalization, "clears up" the information of the sense organs, and permits a man to determine correctly the position of his body in space.

G. Titov, after his flight, said that, by tensing the muscles, the disagreeable vestibular-vegetative sensations almost vanished completely. The astronauts Feoktistov and Yegorov were of the same opinion. Obviously, in this case the proprioceptive afferentation with the muscles suppresses the uncommon vestibular signalization. Cutaneous reception must also play a definite role in this case [14, 15, 22].

We can assume that the illusions and disagreeable vestibular-vegetative phenomena caused by uncommon vestibular signalization (and possibly proprio- and interoceptive signalization) occur more easily because of a general exhaustion of afferential information. Sufficient tonicity of the reticular formation and cerebral cortex are also obviously contributory factors [2]. It is possible that because of this, an increase in the total sum of afferential signals by muscular tensions and impulse activity improves the condition of the astronauts significantly.

Actually, some of the astronauts experienced disagreeable vestibular-vegetative reactions and light symptoms of nausea several

hours after the start and, although these symptoms did not prevent carrying out the work planned, they did last almost throughout the entire flight. However, the condition of the astronauts improved greatly after sleep. P. Belyayev and A. Leonov, who carried out particularly active work connected with remarkable nervous-emotional and physical strain, did not experience these disagreeable sensations.

Thus, together with the phenomena of adaptation, restructuring the nervous system adequately by new gravitational conditions, the phenomena of cumulation of disagreeable signals, and in the cases known, the collapse of adaptation mechanisms take place. The state of tonicity of the central nervous system is of immense importance, as was indicated by the improvement in condition after sleep, after resting the nervous system.

In this sense, the level of the working apparatus shows up significantly in the reactions of the astronauts' organism. Under known conditions, the effective dominance is a serious normalizing factor. Thus, despite the unusualness of the conditions of flight and "emergence" into space (for example, while Leonov was locked outside the craft), the working apparatus very clearly "suppressed" the disagreeable sensations and problems of orientation in space, connected with the state of weightlessness, which were possible in this case. /29

Illusions regarding the position in space are obviously the result of uncommon interactions of the analyzers, uncommon combinations of signals with various receptors. This can be a result of the fact that the weight of the body and the subjects has been lost, and the mass, and thus their inertial properties, are preserved. The illusions are lost when a new coordination of information from various analyzers is selected, so that the astronaut can be correctly oriented in space. These illusions seem to be a symptom of a transitional period from one type of coordination in the analyzer region to another.

The uncommon signal coming from the receptors of inner organs, the uncommon combinations of signals among various interoceptive zones, and among interoproprio- and exteroceptive zones as well, also play a definite role in the occurrence of vestibular-vegetative problems and illusions [1, 27, 49]. These examples show that the analyzer activity of the central nervous system under conditions of weightlessness can be best understood in the light of Orbeli's study of the interaction of afferential systems, in which this interaction is understood as a plastic functional systemization in the work of analyzers, which has great possibilities for constructing new coordinations and which as a result facilitates a more complete and reliable reflection, under these conditions, of the external and internal (visceral) world in our consciousness [19, 23].

EFFECTOR SPHERE, COORDINATION OF MOVEMENTS

Both changing mechanical conditions (the lack of weight with conservation of mass and thus of inertial phenomena) and changing afferentation, which complicates correcting the movements according to the principle of feedback, have an effect on coordination of the movements. The adapting and perception-tonic reflexes, on whose foundation all other movement coordinations are built, change under the conditions of weightlessness. Moreover, a lack of reference points in outer space creates completely new conditions which are uncommon for biomechanics.

The results of studies completed during short-lived weightlessness on aircraft, and under conditions of acceleration as well, showed great possibilities for compensation and rapid restoration of coordinating basic movements [18, 24, 37, 41, 42, 50]. The astronauts' handwriting also improved significantly from loop to loop [12, 21, 25].

In our opinion, the possibilities of carrying out complex actions which are under the control of the cerebral cortex and which have great possibilities for adaptation, compensation, and representation, must be even more advantageous. /30

Actually, the astronauts on board "Voskhod" and "Voskhod-2" had no difficulty in carrying out the duties assigned to them. There were no complications noticed in coordination of movements. However, an analysis of the time spent in fulfilling a number of operations (work with instruments, plethysmometry, etc.) showed that, at the beginning of the flight, we could anticipate a certain increase in this time relative to standards on Earth or to that time required for the astronaut to complete these operations in subsequent orbits of the flight.

Thus, for example, on his first turn, V. Komarov, while executing certain duties, connected with orientation of the craft, spent about twice as much time as during subsequent revolutions or on Earth. Yegorov also noticed this in carrying out physiological measurements. It is quite possible that this phenomenon can be explained by the effect of "external decceleration" as a result of the novelty of the situation and of the restructuring of habits relative to the conditions of weightlessness. In subsequent orbits of the flight, these phenomena, as a rule, are smoothed out and compensated.

A study of the resolving power of the optical analyzer (taking the non-standard lighting conditions into account) did not reveal any significant changes. The operating optical efficiency decreased in a number of cases, but not to any significant degree.

A study of the dynamic characteristics of the operator in a model control system seemed very interesting. Step-shaped, random,

and sinusoidal signals with certain rate responses were used. The operator (astronaut) had the possibility of regulating the controls by direct and indirect feedback in the system. It was found that, in comparison with the data obtained during conditioning in the experimental model craft, the mean square error of the operator under flight conditions increases more significantly at high rate of the signal presented.

Yegorov also came to the conclusion that the dynamics of well-developed habits for carrying out the programmed operations were not disrupted at all.

Thus the data obtained indicate that the cosmonauts maintained a sufficient level of efficiency during the flight to ensure total /31
fulfillment of the many-sided flight program.

An analysis of the conduct and movements of Leonov while he was outside the craft is of special interest. These data are an important factor in clarifying the possibilities for carrying out various work functions in the future (assembling objects in space, for example). It is interesting that, under conditions of weightlessness, it takes little exertion to rotate the body in various planes at a fairly high angular velocity. The results of motion-picture filming during the astronaut's walk confirm this assumption.

A preliminary biomechanical analysis of the characteristics of Leonov's movements while he was outside the craft (and during studies on Earth in a special test unit as well) indicates a completely satisfactory coordination of movements and the possibility of carrying out many adjustments and movements with the aid of an umbilical. The astronaut knew how to carry out the necessary actions to prepare the movie-camera for operation and to dismantle it before returning into the craft. All the operations were completed manually with no complications. These data are greatly encouraging from the point of view of the possibilities for man to carry out operations outside a spacecraft.

It is most probable that, in selecting astronauts, consideration of their individual abilities to rebuild coordinations in afferent as well as efferent spheres was very significant. It is important to develop the training correctly, in order that the ability to rebuild coordinations may develop more greatly.

We are suggesting that, in studying the possibilities for rebuilding the given coordinations and replacing some by others, the work of Orbeli and his school [23] on the mechanisms for rebuilding coordinations, on how (in rebuilding biologically new coordinations) the old coordinations are suppressed and how their separate elements are used in part, can be of great aid. Special attention should be paid to the cerebellum in this case. Orbeli considered that one of the functions of the cerebellum is the suppression of old coordinations for building new ones. In order to understand the mechanism

for building new coordinations under the uncommon conditions of gravitation, the works of N.A. Bernstein on building movements and the role of various levels of the nervous system in it [9] also have great significance.

SPHERE OF REGULATION OF THE VEGETATIVE FUNCTIONS

The state of weightlessness, as we noted earlier, can be exerted on the vegetative functions both as a direct influence as a mechanical factor and as a reflex effect with reflexogenic zones. /32
But the main concern, as we have suggested, is the destruction of coordinations and the system of self-regulation of the vegetative functions.

For example, let us examine the cardiovascular system.

Losses of weight in blood can be caused by incorrect information from the mechanoreceptors of the vascular canal under the condition of hyperemia of the corresponding section of the vascular canal which, in turn, results in an inadequate reflex reaction, inadequate redistribution of the blood and unfavorable conditions for the operation of the heart. Losses in the "vertical" of an organism can result in the pressure gradient in the vascular canal losing one of its values. It is probable that the appearance of a third cycle for the astronauts' seismo-cardiogram [12] described earlier by one of us (O. Gazenko) is connected with these stresses in intracardiac hemodynamics.

For the majority of astonauts, after active participation in a flight, their pulse rate and respiration returned to the original figures rather rapidly. Subsequently, after 2 or 3 revolutions, it was noted that the pulse rate tended to decrease below the original level. This was noticed in particular during sleep. For example, Yegorov's pulse during the flight reached 46 beats/min. It is true that his pulse on Earth during sleep sometimes decreased to 52, which would imply a certain vagatonic reaction. This is also indicated by a certain elongation of the auriculoventricular conductivity.

In a number of space flights, a decrease in the maximum arterial pressure was registered. In particular, Yegorov noticed this in his colleagues. Thus Komarov's maximum arterial pressure decreased to 95 mm Hg as opposed to 115 mm Hg before the start, and the minimum pressure, on the other hand, increased from 65 to 80 mm Hg. The decrease in the maximum arterial pressure and the tendency for the minimal pressure to increase resulted in a certain decrease in the astronauts' pulse pressure.

However, the tendency of the pulse rate to oscillate attracts the most attention. For example, for almost all the astronauts the reaction to the transition from sleep to wakefulness is characterized by a short-lived increase in pulse rate with a subsequent

decrease and by longer-term disturbances on the part of the systolic indicater, the time for auriculoventricular conductivity, and by a decrease in the electric systole as well.

The astronauts on board "Voskhod" and "Voskhod-2" noted that even moderate physical stress resulted in a noticeable tendency to perspire and sometimes in increased fatigue.

All this obviously indicates disturbances in regulating the vegetative functions in a state of weightlessness, some instability in the new coordination or regulation of the vegetative functions, and dystonia, or an unstable balance between the sympathetic and parasympathetic parts of the vegetative nervous system. Gazenko earlier presented a physiological interpretation of these phenomena /33 in a discussion at the IIIrd Symposium on Bioastronautics in Texas, in November, 1964. The results obtained have stimulated further studies relative to more prolonged flights, in particular.

We should note, however, that for the cosmonauts on board "Voskhod-2" there were noted certain special characteristics of the physiological reactions which differed from those observed in all the preceding flights. After the craft went into orbit, the rate of Belyayev's and Leonov's cardiac contractions continued to increase somewhat further: there was noticed a moderate tachycardia (Fig. 1). This was obviously linked with the accomplishment of a complex of planned operations which provided for the second astronaut's walk in space. In this case, respiration also increased significantly. The similar nature of the reactions in general conforms with that observed during training operations with a simulation of the walk on Earth.

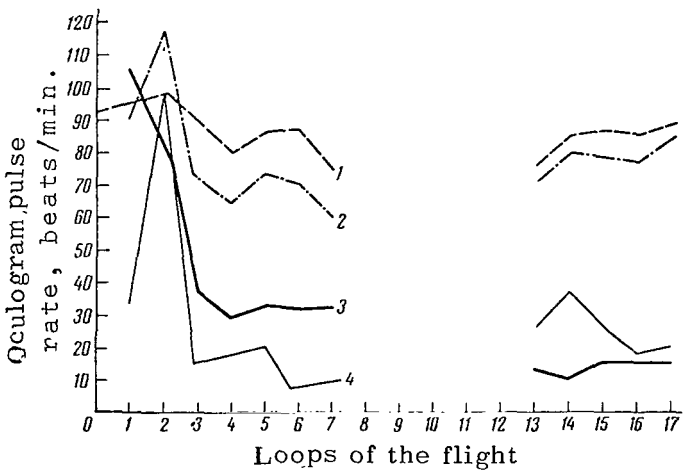

Fig. 1. Pulse Rate and Oculogram during Leonov's and Belyayev's Flight. (1) Belyayev's Pulse; (2) Leonov's Pulse' (3) Belyayev's Oculogram; (4) Leonov's Oculogram

Examination of the oculogram for Belyayev and Leonov during flight showed a high rate of eyeball movements during the period from the first to the fourth loops, which also obviously indicated the significant activity of the astronauts in that orbit of the flight (Fig. 1).

At the moment of Leonov's exit, and while he was outside the craft, his pulse rate and respiration increased, this being easily linked with natural emotional tension. In fact, after returning inside the craft, these indicators were rapidly normalized. Thus, /34 at the end of the "exit" period, Leonov's pulse rate became equal to 100-120/min and corresponded to the values noted during similar training on Earth; at the moment of his exit it increased to 150-160; while entering the lock, when an astronaut undergoes certain difficulties, his pulse rate reached 168; after having entered the lock, his pulse rate decreased fairly rapidly to 100-120 (Fig. 2).

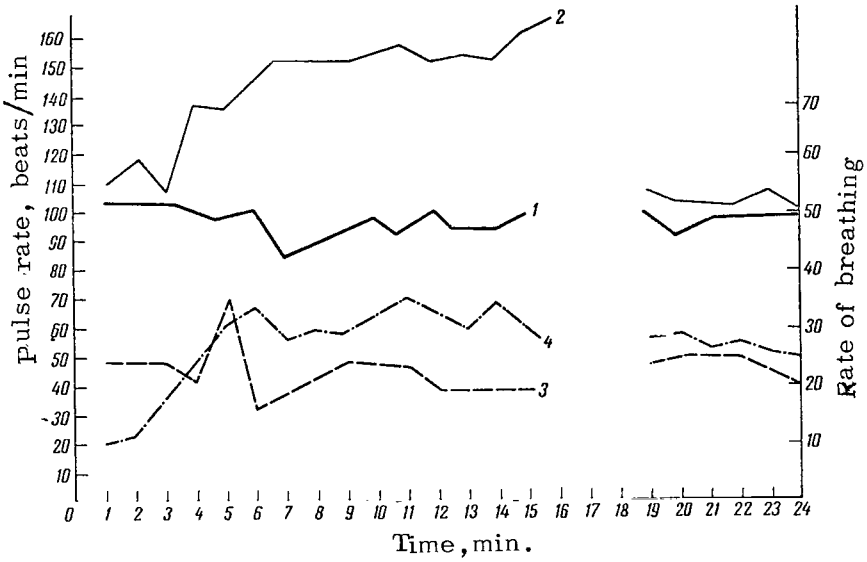

Fig. 2. Leonov's and Belyayev's Pulse Rate and Respiration during Leonov's Emergence into Outer Space. (1) Belyayev's Pulse Rate (2) Leonov's Pulse Rate; (3) Belyayev's Respiration; (4) Leonov's Respiration.

An analysis of blood tests for Feoktistov and Yegorov taken at the 2nd and 12th loops of the flight of "Voskhod" did not show any changes in the carbohydrate and salt metabolism. A certain increase in the percentage of urea in the blood - up to 41-51 mg% (while during control tests it did not once exceed 40 mg%) - was also noted. This obviously indicates a somewhat increased decomposition of proteins under flight conditions. Moreover, a leukocytosis was also noted in Yegorov.

The pulmonary ventilation of the cosmonauts increased significantly during the flight. For example, it increased by a factor of 2-3 for Belyayev and Leonov. The need for oxygen changed ambiguously, thus preventing definite conclusions. /35

A comparison of the physiological data registered during flights of varied length (for the craft "Vostok") with data from the flights of 3 astronauts ("Voskhod") and 2 astronauts ("Voskhod-2") aids us in evaluating the significance of emotional stress within the framework of physiological reactions, the significance of individual psychophysiological characteristics of the astronauts, and the factor of flight length.

It seems that the indicators characterizing the state of the cardiovascular and respiratory systems for the crews of "Voskhod" and "Voskhod-2" in the pre-launch period, and during active participation in the flight, changed to a lesser degree than for the astronauts who had previously completed flights on "Vostok". Thus, for example, if the pulse rate for V. Bykovskiy during active participation was 137/min. and for V. Tereshkova it was 151, then for Komarov, Feoktistov and Yegorov it was equal to 98, 102, and 109/min. respectively (Table 1). Transition from excess gravity to weightlessness was smooth, and, as the astronauts said, "imperceptible".

TABLE 1. CHANGE IN PULSE RATE FOR THE ASTRONAUTS DURING FLIGHT (IN PERCENT OF THE ORIGINAL LEVEL).

Craft	Astronauts	Pulse Rate, beats/min.			
		Original Level	Before Launch		Active Participation
			5 min.	1 min.	
Vostok-5	V. Bykovskiy	64	207	226	214
Vostok-6	V. Tereshkova	78	162	178	194
Voskhod	V. Komarov	72	152	124	136
Voskhod	K. Feoktistov	76	118	126	134
Voskhod	B. Yegorov	63	136	149	175

Thus space flights carrying a crew obviously have definite superiority over solitary flights, from medical and physiological reactions in practically all orbits of the flight and even before launch. It is easy to see the beneficial value in the "feeling of fellowship" from the data presented.

Twenty-four hours after the flight, functional cardiovascular tests (passive orthostatic test, test with proportioned physical excess gravity) allowed us to find certain special characteristics of the reactions. Thus the reaction to excess gravity was somewhat more expressed, and the recovery period lasted longer than before the flight. The shock and minute volumes also decreased somewhat (for Feoktistov and Yegorov by 26-47%), and the pulse pressure decreased (by 10-24 mm Hg). For Yegorov after the /36

functional test, a decrease in the arterial pressure was noted.

Biochemical studies on the blood after the flight showed an increase in cholesterol. For example, the night after the flight of the astronauts on the "Voskhod", the percentage of cholesterol reached 260-290 mg% instead of the 120-180 mg% which was normal for them. The next morning, it had already dropped to 220-260 mg%, and had completely returned to its original value after 2 weeks.

These data probably indicate a certain tension in the lipoid metabolism, and the possibility for a fairly prolonged period of after-effects as well.

Studies of the sugar content in the blood of the astronauts on the "Voskhod" after the flight showed great individual peculiarities. Thus, for example, low sugar concentrations were characteristic for Yegorov, and, on the contrary, somewhat increased concentrations for Komarov. A study of the amount of ketocoricosteroids and of the indicator of the K/Na ratio in the urine did not reveal any serious divergences from the norm. However, these results were obtained after a day-long flight, and we could anticipate a stronger reaction for longer-term flights.

The day following his flight, Belyayev's energy expenditure exceeded the original value by 29%, but only by 13% for Leonov.

Two days after their flight, a functional study of Komarov's and Yegorov's kidneys was conducted by the method of water volume. It was found that the removal of water from the organism was decelerated in comparison with the results of analogous studies before the flight and 2 weeks after it. In this case, the astronauts had no breakdowns in the glomerulus filtration, and the concentration capacity of the kidneys did not develop. We should note that the astronauts did not experience thirst during flight, although the losses in water were fairly significant. Immediately after landing, they felt a strong thirst. It is probable that these changes were caused by nervous-emotional tension and hormonal stresses occurring during the astronauts' flight. In particular, this breakdown of the water-excretory function could be connected with secretion of an antidiuretic hormone.

The changes involving energy expenditure and water metabolism give us supplementary material for explaining the well-known phenomenon of the astronauts' weight loss after the flight. The weight of the astronauts on "Voskhod" and "Voskhod-2" as a result of the flight decreased by 1-3 kg; for Komarov, by 1.9; for Feoktsitov by 2.9; for Yegorov by 3; for Belyayev by 1.0; and for Leonov by 0.9 kg. /37

These data show that, under the conditions of weightlessness, the primary physiological effects are not local changes (for example, humoral changes) but breakdowns in the general nerve-reflex

regulation and self-regulation. The origin of this whole series of changes is the change in signals from the receptors and primarily of the cardiovascular system. The changes in the character of signalization from the vascular receptors, as we know, can cause radical changes in the regulation of blood circulation [44, 48]. The latter results in breakdowns of the environmental stability which is necessary for specific activity of various tissues, and in breakdowns of the tissue metabolism as well.

The results of the post-flight examination show that the functional stresses and the instability of regulation for the vegetative functions (found during tests with weight in particular) can be observed for some time after the flight.

In relation to this, it would be appropriate to be reminded of the special characteristics of the reaction of the organism of an astronaut during transition from acceleration to weightlessness and from weightlessness to acceleration [12, 20, 51, 52, 58]. During transition from weightlessness to acceleration, the resistance to excess gravity of an organism which is in a state of instable rebuilding of the vegetative functions would probably be weakened. In fact, the astronauts repeatedly insisted that the accelerations during return to Earth were more unbearable then during entry into orbit [12, 55, 58].

During an astronaut's active participation in the flight, his pulse rate and respiration significantly exceeded those which were noted during the effect of similar conditions in a centrifuge. The time for the return of these indicators to the original level after the end of the effect of accelerations in the space flight, as has already been explained some time ago, [9, 12, 35, 58] exceeded by a large factor the corresponding values during studies in a centrifuge on Earth. This period was particularly prolonged during the flight of "Voskhod-2", which we stated earlier in connection with the astronauts' problems in preparing for the "walk" in space.

All this indicates that the reactions of the organism of the astronauts relates to a whole complex of causes, of factors influencing them. In this case, we should consider the qualitative and quantitative features of the influence on an organism of a combination of a number of simultaneously influencing factors, the significance of the definite after-effect of the influence of various factors, and also the significance of the entire complex of external and internal conditions, among which the condition of the organism, and in particular its nervous system before preparation for conditioning, play an important role. By this example we can be convinced that it is not sufficient to be limited to the study /38
of the influence on an organism of separate factors of flight, but that a synthetic evaluation of their entire complex is necessary [11, 54]. The problem we touched upon is very timely and requires special study that goes beyond the limits of this paper.

Thus we see here the expediency for applying the synthetic principle in studying the physiological effects of gravitation [14, 23, 26, 54].

SEVERAL GENERAL CONCLUSIONS

Analysis of the above data, in our opinion, allows us to draw certain preliminary conclusions.

The effect of weightlessness, as a mechanical factor applied directly during physiological processes, is most likely not very important.

The changes in the receptor functions and in the region of afferentation are of primary importance.

The afferentation, which is uncommon because of its general quantity and composition, causes the following basic groups of reactions:

- a general non-specific stress-reaction;

- breakdowns in perception by external and internal (intero- and proprioceptive signalization) analyzers which result in illusions (including the breakdown of spatial orientation and spatial analysis);

- inadequate reactions on the part of internal organs, breakdown of self-regulation and coordination of the vegetative functions; the so-called vestibular-vegetative breakdowns;

- breakdowns in coordination of movements and decrease in operational efficiency.

Immediately after the transition to weightlessness, the following mechanisms for adaptation of an organism to uncommon gravitational conditions, mechanisms for compensation and representation of the collapsing and dying-out functions, appear.

- Mechanisms of non-specific afferentation, which are closely related to the stress-reaction;

- Rebuilding in the sphere of afferentation; new coordination of activity for the analyzers, which results in a possibly more complete and reliable reflection of the world under the uncommon conditions of gravitation; this rebuilding is done under control and, because of corrections by higher sections of the central nervous system, with the cerebral cortex, in particular:

- Rebuilding by regulation of the activity of inner organs; new coordination of their activity, in order to guarantee stability in the environment and the functional possibilities of the organism

(in this case, orbits of more or less complete compensation for the functions which have broken down are observed); however, even with satisfactory compensation, the reserve possibilities for the organism are somewhat limited (which is seen by applying excess gravity), and the new coordination is somewhat inadequate (at least during short flights); /39

- Rebuilding in the domain of somatic functions; the new coordination of movements is done under control and with a great amount of participation by the higher sections of the central nervous system; preliminary preparation and conditioning plays an important role; in this case, compensation (adaptation, representation) is guaranteed for elementary habits as well as for complicated types of activity; there are symptoms, however, which indicate that the compensation is not always complete (at least during short flights).

SEVERAL RECOMMENDATIONS

The prospects of more distant and prolonged flights in space, in which the astronaut will have the complex duties of pilot and researcher, require development of the corresponding practical methods for selecting and preparing the astronauts, and for producing optimal conditions and regimes for their work and for preventive and safety measures.

The following are necessary for solving this problem:

1. A profound and systematic study of the effect on an astronaut of flight factors (weightlessness, in particular) and of the mechanisms of adaptation to them would entail foreseeing the organism's reaction under the conditions of various itineraries in space, and to plan the flight program, the duties of the astronaut, and safety measures correctly.

2. In selecting astronaut candidates, obviously, we must consider the individual characteristics of the plasticity and motility of the nervous system, its possibilities, in correspondence with the new environmental conditions to rebuild the old coordinations in the afferent and efferent domains and also in the activity of the internal organs; in preparing the astronauts, these abilities must be developed more.

3. We must study the role of separate parts of the central nervous system (for example, the cerebellum, the sympathetic nervous system, and others) in rebuilding coordinations adequate for the environmental conditions, we must also study the possibilities of pharmacological effects or any others which might aid in linking this rebuilding.

4. We must use the possibilities for non-specific conditioning and increase the adaptive capacities of a man, for example, who lives in a mountainous region [5, 47].

5. We must develop rational methods for training and conditioning, which would aid in rebuilding the organism adequately for conditions of the flight. An example of this could be Leonov's training to be oriented in space with the aid of artificial orienting-coordinates, or the planned creation of some operational dominance which would prevent the occurrence of vestibular-vegetative breakdowns. /40

We are suggesting that only the first steps have been taken on this path. The road ahead is long and difficult, but extremely interesting and, we can hope, a fruitful work which promises solution to the problems that are important for astronautics and, at the same time, exceptionally interesting for studying the theoretical problems in biology and medicine. And this is a goal which deserves the fellowship and collaboration of scientists in every country.

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THE PROBLEM OF GATHERING DIAGNOSTIC INFORMATION UNDER THE CONDITIONS OF A SPACE FLIGHT AS ONE OF THE TRENDS IN MEDICAL CYBERNETICS†

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ABSTRACT: New concepts on gathering diagnostic information under the conditions of a space flight are examined in this article as one of the trends in medical cybernetics. The term "physiological measuring-informational system" is proposed, and four important aspects of this problem are selected. New promises are presented for developing systems for gathering diagnostic information relative to space flights continued for a great length of time, using on-board calculating devices, and constructing effective diagnostic algorithms on the basis of treating a limited volume of physiological data.

One important problem in modern space medicine entails collecting the diagnostic information necessary for guaranteeing safety in space flights. In order to solve this problem, we are using the very latest achievements in science and technology in the areas of radioelectronics, biotelemetry, energetics, etc. The development of medical cybernetics has allowed us to introduce new concepts on gathering diagnostic information under the conditions of a space flight. The examination of these concepts is the subject of this article. /42

First of all, we should mention that the system for gathering medical (especially physiological) information on board a spacecraft can entail a number of complex cybernetic systems in which the transmission, reception, collection, and processing of information occur. We are proposing the term "physiological measuring-informational system", which emphasizes the following four important aspects of the problem: *physiological* - for natural solution to physiological (medical, diagnostic) problems; *measuring* - connected with a quantitative evaluation of the physiological processes;

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informational - examining the data circulating in the system as control and communication signals; and, finally, the aspect which emphasizes the necessity for a specially organized *system*, whose elements would consist of a complex of media which provide for obtaining a maximum volume of information on the physiological condition of the astronaut. In a very general way, the physiological measuring-informational system can consist of an information source /43
with onboard and terrestrial equipment, an information receiver, and communication channels. That part of the data which comes from the information source (the astronaut) to the information receiver (the doctor), processed for the solutions and controls which are directly connected with guaranteeing flight safety, can be called diagnostic information. In this case, the time for an information cycle, i.e., the time from the moment of the appearance of data from the astronaut into the measuring system to the moment they are obtained by the measuring system or the spacecraft's control system, is of very great significance. It is clear that, under the conditions of a space flight, the time for circulating information must be minimum. On the basis of the concepts for the physiological measuring-informational system, we can examine the following three problems in sequence: developing systems for gathering diagnostic information relative to a very long space flight; using onboard calculating devices; constructing algorithms for processing the information.

During flights by Soviet and American astronauts, the systems for collecting physiological data counted mainly on solution to problems by medical supervision. In selecting the measured parameters and designing the electronic equipment, the principal goal was that an astronaut's condition be evaluated during the time he was in orbit and, when necessary, that he be given medical aid. The problem of gathering a greater amount of scientific information which would be of interest for predicting the astronauts' reactions and for planning the programs for further flight experiments was solved simultaneously [20]. However, this task, as we see it, was considered secondary. The transition to longer-period and longer-range space flights forces us to examine the second problem on the same level with the problems of medical control. The fact is that, during a lengthy flight, a rather accurate prediction of dangerous devergences in the astronaut's condition cannot be made only on the basis of the data obtained during experiments on Earth, or on the basis of the limited information recorded during the flight. It is necessary that the results of periodically developed medical studies be processed for diagnostic criteria, in order that the operative medical control be instantaneous. Here, the problems of obtaining information are closely connected with developing effective diagnostic algorithms.

The development of a system for gathering physiological information during long-period and long-range flights includes solution to the following problems: obtaining a maximum volume of data while using a minimum amount of equipment; transmitting a maximum volume /44

of data by a telemetric channel with limited capacity; decreasing the time for processing the information.

The last problem involves two circumstances: the necessity for rapid solutions in the system of the operative medical control, and the necessity for rapid re-coding of a large amount of scientific data into concrete diagnostic criteria which can be used for increasing the flight safety. The presence of a doctor as a member of the space crew does not simplify the problem being examined, since the doctor's preparations, the possibility of his processing the information, and his responsibility have definite limits [19].

The problems of the optimal structure for the physiological measuring systems on board a spacecraft have been examined by us in a number of studies [11, 17, 18]. One of the new principles we presented was the separation of two individual onboard measuring systems: one for medical control, and the other for medical studies.

The system of medical control is a somewhat simplified version of the physiological measuring systems now working in the craft "Vostok", "Voskhod", "Mercury", and "Gemini". It is intended for recording a small amount of data, enough for detecting and recognizing such rapidly or suddenly appearing acute disturbances (conditions) as shock, collapse, acute cardiovascular insufficiency, etc. In this case, it is necessary to record two or three physiological parameters as continuously as possible. In the future, this will be done by using a telemetric system within the cabin, which allows for medical control while the astronauts move about freely throughout different sections of the spacecraft. The system for medical studies must have a somewhat greater number of channels, since its significance consists in collecting detailed data on the condition of various physiological functions of the astronaut's organism. However, because of the limits to the weight, bulk, and energy requirements for the onboard equipment, it is difficult to count on maintaining an essential principle: each parameter must have its own measuring channel. We are proposing the principle of a multi-purpose usage of the channels. Each channel can be used repeatedly, connecting various pickups to it, and, if necessary, changing its technical characteristics. This could provide for recording 25-30 and more physiological parameters in 6-8 channels.

The recording of data in the system for medical studies is made feasible by special programs, each of which is intended for studying a definite physiological system of the organism. The effectiveness of the program is determined as the selection of parameters, as well as the introduction into its composition of a collection of functional flights. In addition to the specialized programs, we can use general-medical ones, whose task is to sum up the condition of the organism's principal systems: cardiovascular, respiratory, neuromuscular, and central nervous. The multi-purpose usage of the channels in conjunction with the principle of programmed /45

studies guarantees obtaining a maximum volume of data with minimum onboard equipment.

The principles recommended above for constructing an onboard medical apparatus were tested during the flight of the Soviet multi-seat spacecraft "Voskhod". The medical control was made with the aid of a special block intended for continuous recording of three characteristics (electrocardiograms, seismocardiograms, and pneumonograms) for each of the three astronauts. For the medical studies, we used a separate instrument which provided for recording four different parameters (electroencephalogram, electro-oculogram, dynamics recording, and recording of motor acts) in sequence on one channel. These parameters were recorded by the corresponding program, which included the necessary functional tests. The experimental data obtained substantiate the effectiveness of the recommended system for physiological measurements.

An increase in the length and the distance of the space flights causes a substantial decrease in the amount of data transmitted to the Earth from the craft, which is caused by a sharp decrease in the transmitting capacity of the telemetric channels. During the flights of the Soviet spacecraft, we studied the possibility of "contracting" the information during transmission by the telemetric channels: the "envelope" of a phonocardiogram was recorded [3], and there was transmission of two parameters by one channel [1]. However, effective use of the telemetric channels with limited capacity for transmitting a maximum amount of information is possible only by using onboard calculating devices. Since, with an increase in the flight distance, circulation of the information in the "astronaut-craft-Earth" system greatly increases, the appearance of onboard calculating devices has already been prepared for the near future by all the developments in space technology. Such devices, together with technical tasks (orbital calculations, regulating the systems for life-guarantee, automatic orientation, etc.), will also solve the problems of automatic medical control [4, 23, 24] as well as the problems for programmed collection of scientific and diagnostic information, both for "contraction" of the data for transmission to the Earth by telemetric channels with limited capacity and for preservation in the onboard memory systems. When a doctor is present as a member of the crew, the onboard calculating device can aid, in addition to carrying out an automatic signalization of dangerous conditions, in carrying out the role of a "diagnostic machine"-counselor. /46

When there is an onboard calculating device, there is a new physiological measuring-informational system which is independent of the Earth. This system requires giving principal significance to guaranteeing the safety of the space flight with time, and the "Earth" maintains the role only of a consultant and collector of scientific information. The operation in the area of onboard calculating devices is of great interest in space medicine. It is part of the general-medical problem of "diagnostic machines". In

space medicine, we should use "diagnostic machines for conditions" [15]. The determination of conditions, or, more accurately, of syndromes, as combinations of individual divergences called symptoms is the basis of any diagnostic process.

The development of diagnostic algorithms and of corresponding programming machines is intended for designing effective diagnostic automatic systems on a spacecraft. A diagnostic algorithm is a strict regulation on the order of the operations of deciphering, analyzing, and calculating the medical information. The process of treating information on the astronaut's condition with solutions connected with flight safety can be effective only if there are concrete algorithms, whether they are carried out automatically or manually, on the Earth or on board the craft We can single out three groups of algorithms: determined, probable, and automatically changing [12]. Today, on the basis of the human reactions we know to the effect of various extremal factors, and on the basis of experiments with short-duration space flights, we can construct mainly determined diagnostic algorithms of the matrix type. As a result of studying clinical models, the possible breakdowns in a lengthy flight, and a theoretical analysis of the conditions for a lengthy flight, we can develop more effective probability algorithms. Such algorithms provide for greatly increasing the quality of the solutions by a great increase in the volume of input information (here we are considering the collection of supplementary data with the aid of the system for medical studies).

Finally, the most complete algorithms are the automatically changing ones, which can increase effectiveness with the duration of time. The self-perfection of the algorithms is caused by the system's ability for collecting information, and by the presence of several previously stipulated general principles in the primary algorithm.

A very important problem in programming the onboard diagnostic systems involves determining the minimum necessary amount of input information for realizing the stipulated algorithms. The requirement of a minimum for the input information is caused mainly by the specific conditions for the space flight. The minimum of input /47
data means the minimum of data units on the astronaut, the minimum of electronic equipment on board the craft, and the minimum of energy requirement. However, this does not mean that the reliability of the "diagnosis" should suffer for the sake of satisfying rigid engineering requirements. The presence of an onboard calculating device provides for examining this problem from a different angle - under the banner of the fight against information overflow, and in the direction toward extracting a maximum amount of useful information for minimum volumes of input data.

The construction of effective diagnostic algorithms based on the processing of minimum volumes of input information requires a detailed analysis of the mechanisms for regulating the physiological

functions and detecting in the organism the existing correlations between the various physiological functions and their characteristics. The cybernetic method for studying the mechanisms of regulation in the organism provide for introducing quantitative information and a large number of rules which now have only qualitative characteristics. The systems of a living organism pertain simultaneously to a huge number of regulating parameters. The homeostatic maintenance of the constancy for the internal medium, and the continuous dynamic balance with the exterior medium, are characteristic of the whole system. A living organism is a complex, multi-purpose, hierarchical system which consists of components subject to an organized whole, so that qualitative differences between orders of discipline occurring in sequence produce a definite specific character for each of the levels. The interaction between lower and higher levels of the complex biocybernetic system is based on a change in the information according to the principle of reciprocal communications with regulated thresholds. The features of autonomy are characteristic of the lower levels at certain boundaries. Let us examine a simplified model of a two-component biological system in which one of the elements must be subject to the other. As an example of such an element, we can take: a cell, an organ, or a physiological system. The element of the lower level has the properties of self-regulation, self-direction, and self-control. These properties are the basis of any living system [21]. In order that they be realized, the element of the living system being examined must have the necessary apparatus: devices for receiving and processing information, regulating devices, formulating the corresponding commands, and effector links which carry them out. The element being examined must receive information on the internal as well as the external medium, and its reactions must be directed toward the internal as well as the external world. The second component of the system is on a higher level in relation to the one we just discussed, and is linked with it by channels for direct and inverse communication. The latter fulfills the aims of the control. Obviously, there is no information sent during normal operation of /48
the system by the channel for inverse communication. In the opposite case, the higher levels would suffer from an acceleration of information. Recent studies in the area of the physiology of the reticular formation have shown that the principle of selective choice only of the most important signals is characteristic of the control systems of a living organism, even for the level of the cerebral cortex. Only in the case when the lower element of the system cannot handle the information flow or cannot separate the useful information from the noise do the elements of the higher level interfere with its operation. The interference of the higher levels in the operation of the lower ones occurs in those cases when the organism, as a whole system, is necessary for the development of reactions which will preserve it from breakdown during the action of disadvantageous factors.

In this case, the mechanisms of the higher level preserve their high functional properties because of the acceleration on the lower levels.

For an example of this, let us examine the compensator-adapted reactions of an organism to the effect of accelerations (an active segment of a flight). The experimental data we have provide for separating two levels of compensation mechanisms: corticosomatic and vegetative. It is well known that, during all the space flights, the astronauts were completely conscious for the active segment of the flight, they made communications, carried out the necessary motor acts, and adequately evaluated the situations. At the same time, we noticed a number of expressed shifts in the systems of blood circulation, respiration, and metabolism. The activity of these systems is extraordinarily intensified. There are distortions in the course of certain reflex acts. Thus, with an increase in the pressure in the lesser blood circulation, there is known to be an unloading reflex in the form of bradycardia, a decrease in the arterial pressure in the greater circulation, and deposition of the blood in the spleen (Parin's reflex) [16]. However, during lateral accelerations, the "adequate" response is maintained only in the spleen. According to the data we have, lateral accelerations of 8-12 units cause dogs to have expressed dystrophic changes in the spleen with thrombogenesis and destruction of the trabecullae, which can be the result of an overflow of blood in the spleen [2, 22].

It is well known that the arterial pressure increases when affected by accelerations, and the pulse becomes more frequent. The blocking of a reflex with the pulmonary vessels in greater blood circulation can be explained by the simultaneous appearance in the blood of sympathins which have hypertensive and positive intratropic effects. Thus, the cortical mechanisms have predominance over the vegetative, and they force their reactions, which do not correspond to the general direction of the whole organism's response.

The example introduced shows that a diagnostic algorithm must never be constructed only on the basis of a collection of symptoms which are components of one or another syndrome. Under specific /49
conditions for a space flight, new syndromes are formed; and in order to calculate them correctly, we must know some general principles for the organization and functioning of the biological systems. As we have shown, one of the main principles for the organization of such systems is the formation of a multi-level structure in which the lower levels are subject to the higher ones during the simultaneous presence of autonomous properties of each of them.

Now, we will examine the important functional feature of biological systems - their operational regimes. All the conditions of an organism can be either stationary or transitional. The stationary states are those states which relate to homeostasis, when the individual components of the system are balanced with each other and with the exterior medium. In this case, each of the functional levels (physiological systems) have the greatest degree of autonomy. The transitional states are the reactions of an entire organism or of its individual components to a disturbance (external or internal). In this case, the components of the biological

system have the greatest degree of co-ordination, since in a given case the defensive reaction of the entire organism is necessary and expedient. Since the stationary and transitional states must have a varying degree of constellation for the individual components of the biological system, we can assume that the characteristics of mutual correlation between various parameters of the physiological functions, and the characteristics of the internal correlation in the dynamic series of values for one parameter, must also differ. Thus, we can develop the corresponding mathematical procedures for "diagnosing" the organism's stationary and transitional states. For this purpose, we must examine the physiological meaning of such mathematical characteristics as depressions, automatic- and reciprocal-correlation functions, the sequences of distribution, the differential equations, etc.

The positive results of adding a correlation and spectral analysis to electroencephalography are now well known (9, 14). Data have been published on a physiological calculation of a number of statistical characteristics obtained by analysis of the astronauts' pulse rate [5, 13]. We will give an example here for using the histographic method in order to study the phenomenon of expressed rhythm vibrations of the heart contractions under the conditions of weightlessness. A significant intensification of sinusal arrhythmia during flight tests in orbit with animals and during the first manned flights was discovered [10]. A special statistical study showed that the intensification of sinusal arrhythmia is the result of the relative predominance of the tonus of the parasympathetic section of the vegetative nervous system, occurring as a response to the decrease in the organism's energy processes and a decrease in the afferent impulses [7]. For a more detailed evaluation of the role of sinusal arrhythmis in the organism's reactions to the conditions of weightlessness, we used the histographic method. We constructed a histogram (interval of .05 sec.) by values of 100-150 for sequential measurements of the length of the cardiac cycle. The histogram or the variation curve was characterized by three criteria: its position on the abscissa axis, its width, and its shape. Laboratory studies showed that the variation curves for conditions of relative repose (stationary process) are characterized by their middle position on the abscissa axis, and their width is determined as being within the range of 0.20-0.35 sec., while by shape they are single-peaked, compact curves. During sleep, variation curves of another type were recorded: expansions to 0.50 sec., shifted toward the right-hand side, and sometimes with two peaks. The transitional processes give asymmetrical curves shifted toward the left, and frequently having many peaks. Under the conditions of space flight, we discovered four types of variation curves which mainly correspond to the time-periods for the flight. /50

Before take-off, during the astronauts' active participation in the flight, and during the first loop, the curves were recorded as shifted toward the left, narrowed, and having a sharp peak, which indicated the high degree of inter-relationship between the sinus

node and the central nervous system (sympathetic effect). During the first 5-7 loops, the variation curves gradually took on a regular shape and a middle position. Beginning with the second day of the flight, there was noted a shift of the variation curves toward the right, their expansion, and many peaks. These measurements can be interpreted as the effect of the gradual predominance of parasympathetic effects over the sympathetic ones, as a decrease in the central regulation. Finally, during the 3rd-4th loop of the flight, the variation curves were of a completely specific type: expanded up to 0.8-0.9 sec., with a large number of peaks, flattened. This ovbiously is the result of an autonomous regulation of the rhythm for the heart contractions by one of the lower controlling circuits, without significant participation by the central mechanisms.

The data presented show that a diagnostic algorithm can be developed for calculating the state of central regulation by the blood-circulation apparatus, on the basis of only one parameter - the pulse rate. The problems in extracting a maximum of information from a minimum amount of data have a great significance in constructing effective diagnostic algorithms for programming the onboard calculating devices. In such algorithms, we should use mathematical conversions of very diverse types: dispersion and correlation analysis, construction of curves for distribution of differential equations, methods for information theories and game theories, etc. This, together with the mathematical methods of cybernetic correlations for interpreting the data, gives us very alluring prospects. Thus, there is the principal possibility of determining someechar- /51
acteristics by others on the basis of the reciprocal correlation of the physiological functions. In this case, the greatest number of correlation dependences, obviously, can be observed during the periods of extremal actions, when the degree of organization for the organism's regulating systems increases. It is possible that the functional state of individual systems can be calculated more successfully by the degree of the internal organization of a number of parameters rather than by their absolute values.

Finally, we will present the results of an analysis by seismocardiograms, illustrating a possible method for calculating the degree of internal organization for the mechanisms of the intracardiac hemodynamics by recording a single parameter. It is well known that seismocardiography is a new method for studying the contracting function of the heart. It was first used in Soviet spacecraft, and it is now a compulsory method for the systems of medical control in astronautics, and is used successfully in clinics for examining the sick [6, 8]. A seismocardiogram gives us a representation of the pulse rate, the strength and coordination of heart contractions, and the specific features of the intracardiac hemodynamics, particularly for the lesser blood-circulation. An analysis of the respiratory variations for these characteristics provides for finding the presence of orbit shifts among them. In our opinion, these orbit shifts characterize the degree of internal

organization for the parameters of the blood-circulation apparatus. For this purpose, we can also use the characteristics of the reciprocal organization.

We purposely spent most of our time in discussing the problems connected with the construction of effective diagnostic algorithms on the basis of processing a limited volume of physiological data. We have demonstrated how the application of a number of cybernetic concepts for describing the mechanisms of regulation for the physiological functions provides for obtaining practical results in the form of concrete mathematical methods for treating the data. In relation to the appearance of onboard calculating devices, the problem of gathering diagnostic information under the conditions of a space flight can be solved only when we have effective diagnostic algorithms. The development of such algorithms has a direct relationship with guaranteeing the safety of long-period and long-range space flights. Thus we can say that two relatively new scientific trends - medical cybernetics and space medicine - have joined forces in an area which is of great interest, not only for modern astronautics and the prospects of space research, but also for practical medicine, since it is certain that the achievements and conquests of space can, and must, be used in the interests of all mankind.

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SOME RESULTS OF MEDICAL STUDIES CONDUCTED DURING THE FLIGHT OF THE "VOSKHOD"[1]

Yu. M. Volynkin and P.V. Vasil'yev

ABSTRACT: A general resumé is given for the results of medical studies made with the aid of biotelemetry systems and portable scientific equipment during the flight of the "Voskhod".

The astronauts' physiological reactions at individual stages of the flight are analyzed, and hypotheses on their origin are presented.

It is emphasized that the results of the studies did not reveal any pathological reactions, but provided a possibility for interpreting their individual characters.

The data obtained are analyzed in the light of prospects for the development of astronautics.

Manned flights in spacecraft have their own history, which began successfully on April 12, 1961, with the astronaut Yu. A. Gagarin. /53 By the beginning of 1964, six American and six Soviet manned flights in orbits around the Earth had been completed, with the time spent in space gradually increasing. The total length of time that men could remain under the conditions of weightlessness, up to that time, was equal to more than 435 hours, of which 381 hours belonged to Soviet astronauts. The five-day flight of V.F. Bykovskiy and the three-day flight of the first woman astronaut, V.V. Tereshkova, are of particular interest. The results of the clinical and physiological studies made before, during, and after the flight were reported by us at the Fifth COSPAR Symposium [5].

It is probably difficult to overestimate the significance of an analysis of the medical data obtained with the aid of telemetry during the astronauts' flight. By analyzing these materials, we established a number of rules for the course of an organism's physiological reactions to the effect of flight factors, and we also presented hypotheses which require further experimental confirmation [1, 3, 4, 6, 7, 8].

However, the methods now used for telemetric measurements of physiological functions provide for monitoring only certain characteristics of cardiac activity, the respiratory organs, and the nervous system. Meanwhile, the problems of further medical provisions

[1] A report at the Second International Symposium on the Principal Problems of Human Life in Space. Paris, June 14-18, 1965.

for space flight require a deeper study of human neuropsychological and somatic conditions during flight, as well as the condition of the vegetative functions and the working capacity. Naturally, at the contemporary level of technological equipment, with medical apparatus in the spacecraft, these problems can be solved more simply and effectively by including, as a member of the crew, a well- prepared medical researcher familiar with contemporary clinical and physiological methods.

As we know, a joint flight of three astronauts - V.M. Komarov, K.P. Feoktistov, and B.B. Yegorov - was made on October 12-13, 1964. This flight marked a new stage in man's conquest of space - the stage of space-navigation in spacecraft carrying several men.

The principal problems for medical study during the flight of /54
the "Voskhod" were the following: studying the functional state of the central nervous system and the working capacity of the crew members at various stages of the space flight; studying the effect of a combination of factors in space flight on the functional state of the cardiovascular system and the blood; examining expired air and energy expenditure on the basis of oxygen consumption; evaluating the effectiveness of systems for life-preservation and landing; evaluating the rationality of the stipulated program for the crew members' cycles of activity and rest, under the conditions of space flight.

Certainly, in the course of solving these problems, we encountered a number of difficulties, of an organizational as well as a methodological nature, caused by certain particular features of space flight. We had to make a number of special tests with the aim of perfecting the clinical and physiological methods and adapting them to the specific conditions of operating in a spacecraft.

The methods for medical control and physiological study used during the flight of the "Voskhod" can be conditionally divided into two principal groups:

I. Methods for radiotelemetric measurements of an organism's physiological functions.

II. Methods for clinical and physiological studies carried out by a doctor-astronaut.

Radiotelemetry systems were used periodically to record an electrocardiogram from each astronaut (in the D-S division, a pneumogram (perimeter of the chest), and a seismocardiogram.

The rate of the pulse and respiration were continuously transmitted to measuring sites on Earth.

Moreover, in accordance with the program for telemetric communication, and according to the doctor-astronaut's judgement, an electro-

encephalogram, electro-oculogram, and representation of dynamic and movement coordination were recorded on one channel at random.

During studies in the laboratory and during training in a model craft, the doctor-astronaut developed and carried out during the flight, the following methods for clinical observation and physiological studies: General observations for the condition and behavior of the crew members during various segments of the flight, for the specific features of their reflex reactions, their accuracy in /55
carrying out certain elements of the flight tasks, and their vocal activity; psycho-physiological tests intended for determining the rapidity and accuracy of processing information (correction tables); measurements of the maximum and minimum arterial pressure, examination of the permeability of the blood vessels, plethysmometry; determination of the vestibular apparatus' threshold sensitivity to adequate and inadequate (galvanic current) stimuli; determination of the sharpness of vision and the ability of the eye to focus; preparing stains, and taking blood tests, for calculating the formed elements and for performing biochemical analyses.

In evaluating the astronauts' general condition and their working capacity, in addition to the enumerated data, we examined the quality of the way they conducted the radio conversations, the character and degree of carefulness in their notes in the ship's diary, the results of television observations, their use of the ship's magnetophone, and the quality and number of tasks they carried out during the flight. The pre- and post- flight medical studies of the astronauts were conducted according to the programs we described previously [6, 7].

The flight with the crew on the spacecraft "Voskhod" took place under advantageous radiation conditions: its trajectory was below the limit of the inner radiation belt; the solar activity did not go beyond the limits of its normal values. The craft's maximum distance from the Earth's surface (apogee) was about 409 km, the minimum distance (perigee) was 178 km; the angle of the orbit to the plane of the equator was approximately 65°, and the time required for a complete revolution around the Earth was 90.1 min. The total dose of irradiation, according to individual dosimeters, did not exceed 31 mrad. Such doses, naturally, cannot affect the astronauts' health unfavorably.

For an analysis of physiological reactions during the flight, it is very important to have information on the conditions of the microclimate in the cabin of the spacecraft: the level of the barometric pressure, the temperature of the air, the humidity, and the percentages of oxygen and carbon dioxide.

These parameters of the microclimate were provided for by connecting a reactivation and condition system four hours before launching.

Before the launching of the "Voskhod", the temperature of the air in the cabin was 17°, the relative humidity was 47%, the pressure was 762 mm Hg, the amount of oxygen was about 20%, and the amount of carbon dioxide was about 1%. During the flight, none of the recorded parameters for the microclimate went beyond the permissible limits. Thus, the barometric pressure changed from 762 to 800 mm Hg, the temperature varied from 17 to 22°, the humidity from 47 to 80%, the amount of oxygen from 20 to 22.8%, and the amount of carbon dioxide from 1.0 to 1.5%. /56

An examination of these data shows that the system for reactivation and air-conditioning operated very successfully, and that the astronauts' reactions obviously were not determined by changes in the parameters of the microclimate, but by other flight factors.

One of the important features of this flight was the fact that it was carried out without the use of pressurized suits. Naturally, this significantly simplified the tasks established for the crew members to carry out.

Nourishment for the members of the crew was provided by a supply of rations which were planned with a consideration of the astronauts' individual requirements.

The total energy value of the food taken during the flight was 3400-3700 kcal. In total, the products taken during the flight consisted of about 150 g of protein, 130 g of fat, 430 g of carbohydrates, 200 mg of vitamin C, 100 mg of vitamin P, 10 mg of pantothenic acid, 10 mg of vitamin PP, and about 4 mg each of vitamins B_1, B_2, and B_6. The water system aboard the "Vockhod" was in good working order. The astronauts drank little water, since they preferred fruit juice.

It is interesting to note that despite the fact that the astronauts were completely satisfied in their subjective requirements for food and water, their weight during the flight decreased: Komarov lost 1.9 kg, Feoktistov, 2.9 kg, and Yegorov, 3.0 kg. Specially conducted calculations for perspiration, in particular, (on the basis of determining the percentage of chlorine in the serum albumin) and other data from calculating the water balance in the organism indicate that the decrease in weight occurred mainly because of moisture loss by evaporation, despite the optimum conditions of the microclimate.

The clinical and physiological studies conducted during the flight are of significant interest and great value: firstly because the data from the telemetric studies were first expanded by the observations made by the doctor on board the craft, and, secondly, because the first three astronauts to travel simultaneously were subjected to identical effects of stress factors during space flight, even though one differed from the other in the level of specialized and physical training, the degree of preparation for the space

flight, age, neuropsychological status, and other qualities.

During the pre-launch period, the general condition and attitude of all the astronauts was good. They were convivial, had a high working capacity, adequately reacted to exterior stimuli, and actively and rapidly completed the work activities connected with preparation for the flight.

Their nervous-emotional condition was slightly increased. /57
Their sleep was solid, deep, and refreshing. The characteristics of their vegetative functions were within the limits of their normal individual variations (Table 1).

TABLE 1: DYNAMICS OF THE PULSE RATE, RESPIRATION, AND ARTERIAL PRESSURE FOR THE ASTRONAUTS BEFORE TAKE-OFF.

Date	V.M. Komarov			K.P. Feoktistov			B.B. Yegorov		
	Pulse beats/min	Resp., Rate min.	Art Pres. mm Hg	Pulse, beats/min	Resp., Rate min.	Art. Pres. mm Hg	Pulse beats/min	Resp., Rate min.	Art. Pres. mm Hg
Oct. 1964									
5	76	6-10	115/75	80	12-16	110/75	72	14	100/70
6	76	8-10	110/70	80	14	110/75	60	14	115/65
7	68	6-8	115/75	82	12	110/75	68	11	115/70
8	68	8-12	115/70	84	16	105/75	64	14	105/65
9	68	8-12	110-70	72	12	115/70	60	14	110/70
10	68	6-8	115-70	76	10	115/80	60	16	105/65
11	72	10	120/70	80	18	125/85	64	14	120/70

On the day of the flight, after getting into the craft, all the astronauts remained apparently calm, sure, collected, and showed high efficiency and precise performance. However, as the time for take-off approached, there was a gradual intensification of nervous and emotional tension, expressed in particular by an increase in the pulse and respiration (Fig. 1).

During the last five minutes before take-off, the rate of the heart contractions was greater than on the evening before the flight: Komarov showed an increase of 23%; Feoktistov, 12%; Yegorov, 56%. A similar pattern was noted in their respiration dynamics (Table 2).

It is well known that similar and even more pronounced changes were noted in the astronauts on all previous flights (Fig. 2).

The astronauts took the acceleration effects when the craft entered orbit very well. In this case, they made observations according to the prescribed program, maintained communications with ground stations, and reported their feelings and the passing of commands. The accuracy, rapidity, and adequacy of their reactions to inquiries from Earth indicate that their attention, audial and visual functions, and working capacity remained, on the whole, at a high level. In analyzing the characteristics of the vegetative functions, it /58 is important to note that the maximum increase in the cardiac activity and the respiration occurred during the first 30-40 sec of active participation in the flight, when the acceleration was minimal.

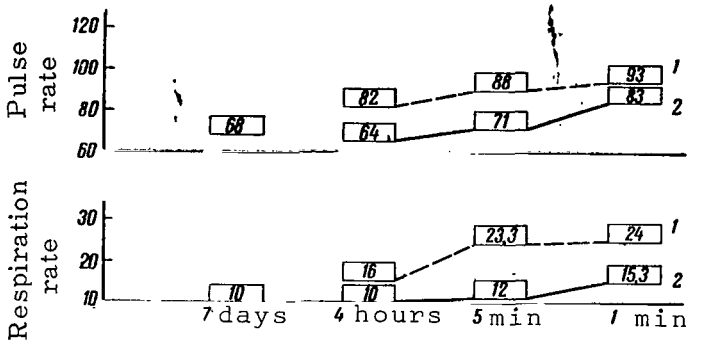

Fig. 1. Change in the Pulse and Respiration Rates of the Astronauts Aboard the "Voskhod" Before Launching (1) and Before Riding a Centrifuge (2) (Averaged Data).

TABLE 2: CHANGE IN THE RATE OF HEART CONTRACTIONS AND RESPIRATION FOR THE ASTRONAUTS IN TAKE-OFF POSITION INSIDE THE CRAFT (EXPRESSED IN PERCENT OF THE ORIGINAL LEVEL)

Astronauts	Evening Before the Flight		In Take-Off Position Before Launching					
	Pulse rate beats/min	Resp. rate min	4 hr.		5 min.		1 min.	
			1	2	1	2	1	2
Yu. A. Gagarin	60	12	108	100	180	175	221	-
G.S. Titov	68	13	101	138	156	115	176	115
A.G. Nikolayev	70	10	102	100	158	100	167	-
P.R. Popovich	50	14	112	143	210	114	270	-
V.F. Bykovskiy	64	12	106	158	207	125	226	158
V.V. Tereshkova	78	12	107	100	162	141	178	108
V.M. Komarov	72	10	121	180	152	230	124	180
K.P. Feoktistov	76	18	102	116	118	111	126	128
B.B. Yegorov	63	14	128	128	136	193	149	193

Subsequently, despite the increase in the magnitude of the overload, the degree of the vegetative reactions, as a rule, decreased

(Fig. 3). Thus there is no relationship between the magnitude of the acceleration and the degree of the increase in the pulse and respiration. In this case, the amount of reaction during the actual flight was much greater than during the simulation of similar accelerations under laboratory conditions in a centrifuge. Having analyzed these materials, we can assume that, of the many factors which are involved when the craft goes into orbit, the one which determines the rate of pulse and respiration is nervous and emotional stress. /59

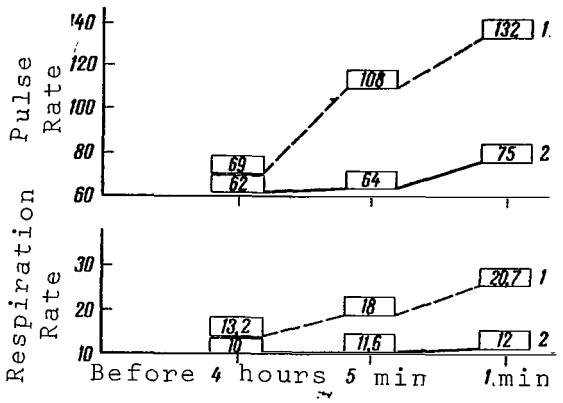

Fig. 2. Change in the Pulse Rate and Respiration for the Astronauts Aboard the "Vostok" Before Take-Off (1) and Before Riding a Centrifuge (2) (Averaged Data).

We should note that the degree of increase in the rate of the heart contractions and respiration for the pronounced individual difference in the last flight was lower than for the conditions of the single flights. This is probably caused by the lesser degree of nervous and psychological tension under the conditions of collective flight, due to the advantageous effect of the crew members on one another.

The transition from acceleration to weightlessness was smooth and, as the astronauts said, "imperceptible". In contrast with Titov's and Popovich's observations, they did not note any illusory phenomena during this period.

When they went into orbit, they had a feeling of "lightness", and their nervous and psychological tension decreased.

In the process of self-observations and medical supervision, it was noted that, under the conditions of weightlessness, the varying degree of physical stress causes a much more rapidly- and sharply- expressed feeling of fatigue, accompanied by increased perspiration.

The crew's working capacity was studied by means of an occupational and graphical analysis of their activity and a calculation of the time spent in carrying out the working operations. /60

An analysis of the tasks carried out during the flight and of the purposeful studies shows that Yegorov's working capacity during flight in orbit was somewhat decreased. In the case of Feoktistov, also, the moral and physical tension involved in carrying out an active experimental operation was much greater than under ground

conditions. As for Komarov, his working capacity remained at a high level during the entire orbital flight.

During this flight, it was again confirmed that a combination of the factors of space flight, mainly weightlessness, has a specific effect on the functional state of the static and kinetic analyzer. This was evidenced by illusory representations of the body's position in space, and also in sensory and vegetative reactions occurring after sharp movements of Yegorov's and Feoktistov's heads. According to the astronauts, the illusions did not interfere with carrying out the prescribed operations; moreover, they appeared only when the astronauts concentrated their attention on their sensations, they then experienced a state of certain discomfort.

It is interesting to note that illusions of an inverted position were noted by Feoktistov and Yegorov when their eyes were open as well as closed, during the entire duration of the effect of weightlessness. The illusory sensations disappeared completely only with the onset of the effect of accelerations during the landing period.

The astronauts' observation that the character and degree of illusions and vertigo were expressed in the same way during free flight as during stabilization (orientation) of the craft, is very important.

Together with the illusions, particularly during the middle of the flight (4th to 8th revolutions), Feoktistov and Yegorov felt unpleasant sensations of a mild, brief vertigo, occurring when the head was turned sharply. Hence, when carrying out the working operations, the astronauts tried to make smoother motions than they did under regular ground conditions.

After 1.5 to 2 hours of flight, Yegorov showed the first signs of vestibular-vegetative reactions, expressed by a decrease of appetite and unpleasant sensations in the epigastric region, which he evaluated as the first symptoms of nausea. These phenomena were expressed more strongly during the 5th revolution.

Feoktistov noted similar symptoms, but they were less expressed. After sleep, this vestibular-vegetative syndrome disappeared almost completely and the astronauts actively continued carrying out flight tasks.

On the basis of an evaluation of all these data, Yegorov considers weightlessness as one of the disadvantageous factors of space flight which requires serious study by doctors. /61

An analysis of the characteristics of the functional state of the cardiovascular system indicates that the general tendency of the changes was not the same as in previous flights. Actually, after pronounced increase in the pulse rate during the period

before launching and during active participation in the flight, even during the beginning period of weightlessness, there is a tendency toward normalization (Fig. 4): for Komarov and Feoktistov, the pulse reached its original level at the end of the first revolution and the beginning of the second revolution; for Yegorov, this occurred at the end of the second and the beginning of the third. Although the normalization of the pulse rate had a pronounced individual character, in each case it occurred more slowly than after riding a centrifuge.

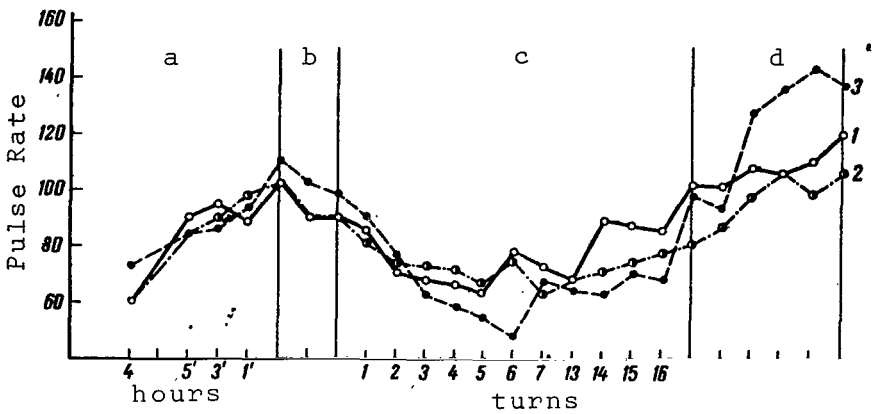

Fig. 3. Dynamics of Pulse Rate for Komarov (1), Feoktistov (2), and Yegorov (3) at Various Stages of Space Flight. (a) Before Launching; (b) During the Active Segment; (c) Orbital Flight; (d) Landing.

During the sixth and seventh resolutions of the orbital flight, while Yegorov was sleeping, a vagatonic reaction was observed: his pulse rate decreased to 46 beats/min. Under the conditions of ground experiments, the rate of his heart contractions during sleep never went lower than 52 beats/min. It is interesting to note that the statistical analysis of the elements of the electrocardiogram, in particular for the R-R intervals, indicates a good rhythmicity in the cardiac activity for the conditions of this flight (Table 3). This fact requires special study, since it does not coincide with what was recorded on previous flights [1].

The blood pressure underwent a two-phase change. During the first revolutions of the flight, there was observed a decrease in the systolic as well as diastolic pressure, and then a subsequent increase.

TABLE 3: RESULTS OF A STATISTICAL ANALYSIS OF A DYNAMIC SERIES OF *R-R* INTERVALS FOR THE ELECTROCARDIOGRAMS OF KOMAROV, FEOKTISTOV, AND YEGOROV, DURING VARIOUS ORBITS OF THE FLIGHT. /62

Characteristics	5 Min. Before Launching	1st	3 rd	6 th	13 th	16 th
		V.M. Komarov				
M (per sec)	0.68	0.72	0.87	0.82	0.87	0.74
δ (per sec)	0.07	0.08	0.098	0.075	0.038	0.043
C (%)	10.5	10.8	11.26	9.14	4.34	5.82
		K.P. Feoktistov				
	5 Min. Before	1st	3rd	6th	13 th	16 th
M (per sec)	0.72	0.75	0.84	0.86	0.93	0.81
δ (per sec)	0.076	0.081	0.084	0.074	0.091	0.053
C (%)	10.56	4.15	9.96	7.66	9.8	6.5
		B.B. Yegorov				
	5 Min. Before	1st	3rd	6th	13 th	16 th
M (per sec)	0.7	0.69	0.94	1.31	1.02	0.96
δ (per sec)	0.073	0.074	0.109	0.044	0.067	0.082
C (%)	10.5	10.74	11.55	3.36	6.58	8.6

Note: *M* is the Average Arithmetical Deviation; δ is the Root-Mean-Square Deviation; *C* is the Coefficient of Variation.

An analysis of the data obtained indicates a definite decrease in the pulse pressure under the conditions of weightlessness.

/63

The rate of respiration for Komarov and Yegorov during the entire flight was somewhat higher than during the day before the flight (Table 4). It is probable that this was caused by a combination of flight factors acting on the background of a certain increase in the percentage of carbon dioxide in the inspired air.

TABLE 4: DYNAMICS OF THE RESPIRATION RATE FOR THE ASTRONAUTS DURING THE FLIGHT ON BOARD THE "VOSKHOD" (AVERAGED DATA).

Astronauts	Before Launching			Craft Entry into Orbit	Orbital Flight (Orbit).					Landing
	Day Bef.	4 hr.	5 min		1st	3rd	6th	13th	16th	
V.M. Komarov	10	18	23	15.8	16.8	19.1	21.8	17.1	18.2	20.1
K.P. Feoktistov	18	21	20	24.5	19.4	18.4	19.3	15.5	15.	17.4
B.B. Yegorov	14	18	27	33.5	26.8	26.8	16	18.8	20.4	25.2

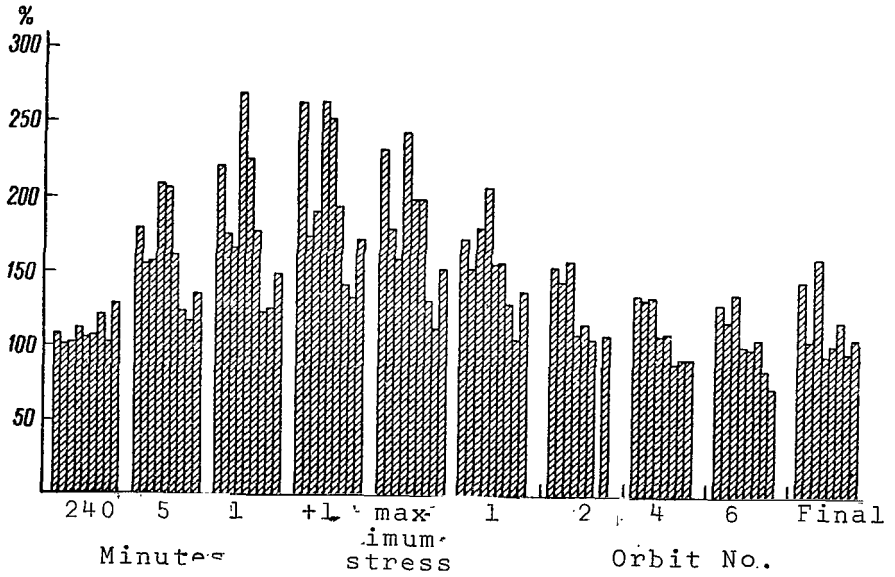

Fig. 4. Comparative Data on Changes in the Pulse Rate for The Astronauts (In Percent of the Original Value) at Various Stages of the Flight in Space. The Columns Correspond to the Sequences of the Flights: Yu.A. Gagarin, G.S. Titov, A.G. Nikolayev, P.R. Popovich, V.F. Bykovskiy, V.V. Tereshkova, V.M. Komarov, K.P. Feoktistov, and B.B. Yegorov.

Unfortunately, because of a breakdown of the instrument intended for studying pulmonary ventilation and gas metabolism, we could not follow the dynamics of energy expenditure under conditions of weightlessness.

In conducting special vestibulometric studies, we did not note any change in the otolith apparatus' threshold of sensitivity to galvanic current; indicatory and graphic tests show that accuracy in carrying out slight coordinated movements decreases under the conditions of weightlessness. This can probably be considered in particular as the result of a change in the functional state of the vestibular analyzer. The post-flight studies did not reveal any substantial changes in the function of the vestibular apparatus. /64

The resolving power of Komarov's eyes did not change, but it decreased for Yegorov. The negative fusion reserves of the outer eye muscles increased by 40-70% for Komarov and Feoktistov, and remained the same for Yegorov.

A calculation of the formed elements of the blood, taken for Feoktistov and Yegorov during the flight, indicates slight leuko- and lympho- cytosis; however, after twenty-four hours, these changes were almost completely compensated.

Biochemical studies showed a certain increase in urea and cholestrol in the blood; this obviously indicates an increase in albumin consumption and tension of the lipid volume.

Actually, in the analyses of the blood tests made during the second and twelfth revolutions for Feoktistov and Yegorov, we discovered 41-51 mg% of urea, while its percentage during the period before launching was always lower than 40 mg%. The night after the flight, and also the next morning, it remained high for all three astronauts.

During the flight, the percentage of sugar and chlorides in the blood did not change. In the blood tests taken on the night after landing, the percentage of cholesterol increased up to 260-290 mg% instead of the 220-260 mg% which was usual.

It is interesting to note that the appearance of the so-called "reaction for preparing to land" (O. Gazenko), characterized by a great increase in the pulse rate, was first observed in the commander of the craft, Komarov (during the 14th revolution), and observed last in Yegorov (at the end of the 16th revolution). The onset of this phase is doubtlessly linked with an increase in the nervous and emotional tension induced by the responsibility for maintaining safety during the final stage of the flight (Table 5).

According to their subjective evaluation, all the astronauts endured the landing phase with more difficulty than the effects of stress, which are similar in magnitude and time in a centrifuge.

This can probably be explained mainly by their previous experience under the conditions of weightlessness for twenty-four hours.

We should note that, during this flight period, Komarov's Feoktistov's, and Yegorov's vegetative reactions were much less pronounced than for the astronauts in all the preceding flights. Actually, Titov's pulse rate during landing reached 156, Nikolayev's reached 148, Popovich's reached 162, Bykovskiy's reached 160, and Tereshkova's was 178 beats/min.

The landing of the "Voskhod" on solid ground was done with the aid of a special landing system at practically zero velocity.

TABLE 5: RATES OF THE ASTRONAUTS' PULSE AND RESPIRATION FOR THE EFFECT OF ACCELERATIONS DURING THE LANDING OF THE "VOSKHOD" AND DURING ROTATION IN A CENTRIFUGE (CF). /65

Characteristics	V.M. Komarov			K.P. Feoktistov			B.B. Yegorov		
	CF	Flight	Diff.	CF	Flight	Diff.	CF	Flight	Diff.
Pulse Rate									
Max.	114	108	-6	102	102	0	92	137	+45
Aver.	93	101	+4	88	91	+3	78	100	+22
Resp. Rate									
Max.	6	22	+16	18	18	0	24	30	+6
Aver.	5	20	+15	12	17.4	+5.4	15.7	25.2	+9.5

Note: In the graph with CF, we have shown the data obtained during rotation in a centrifuge, by a graph which reproduces the dynamics of stress involved in landing.

The post-flight medical study began 15 min. after landing.

All the crew members were happily excited, and they readily answered multiple questions. They did not make any complaints regarding the state of their health, except for fatigue.

During the medical examination of Komarov, his rate of respiration was recorded as 12, and his pulse rate as 92-96 beats/min; for Feoktistov, it was 12 and 98-100 beats/min, and for Yegorov, it was 20 and 90-94 beats/min. respectively.

On the electrocardiograms taken on the first day after the flight, there was a decrease in the *T* wave within the limits of 14-50%, and a slight increase (10%) in the systolic characteristic, for Feoktistov. In analyzing the phases of the heart cycle, a constant decrease in the time for expulsion was noted. The electric systole did not change, and the mechanical one decreased by 0.005-0.040 sec.

All the astronauts subjectively underwent a passive orthostatic test during the first days of the flight very successfully. However, when Feoktistov and Yegorov were standing, there was noted a significant decrease of the beat (by 26-47%) and minute volume of the heart. The pulse pressure also decreased by 10-24 mm Hg, and the average dynamic pressure increased in comparison with the pre-flight data.

In conducting a functional test with 30 knee-bends during the day after the flight, all the astronauts showed a greater increase in the pulse rate than during the pre-flight period. Moreover, the time required for Komarov's cardiac activity to be reduced to the original characteristics increased; Yegorov, instead of an increase, showed a decrease in arterial pressure.

In studying the hemodynamics during the third day after the flight, no significant divergences in the reactions of the heart and the vessels to imposed stresses were seen. /66

Thus, the results of a combined study of the cardiovascular system during the post-flight period indicate a certain change in its reactivity and adaptivity to functional stresses; in this case, probably, there is a certain significance to the decrease of the contractibility of the myocardium (inertia and decrease in the beat capacity), a breakdown of the mechanisms for regulating the coordinated activity of the heart and vessels (instability and decrease of the dynamic pressure during physical stress), and a decrease in venous tonus. The indicated shifts can probably be explained by a state of relative hypodynamics under the conditions of weightlessness and the resultant physical fatigue.

As for external respiration, there were no substantial changes noted. The gas exchange increased somewhat for all the astronauts. The daily energy expenditures during rest increased by 6-27%. However, they did not go beyond +6, +13% above the necessary values for the original exchange.

Subsequently, the changes noted in the function of the cardiovascular system and the gas metabolism after the day-long space flight did not exceed the limits for the physiological norm.

Thus, the results of the clinical and physiological studies conducted during and after the flight supplement the information we have on the reaction of a number of functional systems to the effect of factors involved in space flight. They confirmed the fact that the nature and degree of emotional conditions, the changes in the general physical state and the vegetative functions for the astronauts during a day-long flight basically correspond to the condition of the nervous and psychological sphere and the general stress reaction caused by a combination of factors in space flight. All the divergences mentioned had no pathological character, and, during the subsequent clinical studies, a comparatively rapid

return of the physiological characteristics to their original, pre-flight level was observed.

A definite relationship was found between the nervous and emotional and vegetative changes, and the organism's individual nature, the degree of the astronaut's training, the character of the flight, its length, and the make-up of the crew in the spacecraft. In this case, a flight in a one-seat spacecraft is seen as particularly disadvantageous for the nervous and psychological states.

In conclusion, we would say that the data obtained during the flight again confirm the fact that the study of the effect of weightlessness on an organism remains an important problem for space medicine.

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BIOLOGICAL STUDIES ABOARD THE SPACECRAFT "VOSTOK" AND "VOSKHOD"[1]

V.V. Antipov

ABSTRACT: The principal results of biological experiments conducted on 11 recovered spacecraft are examined: An analysis of the completed studies showed that, various flight factors cause disorders in the hereditary structures of different biological materials: cells in the bone-marrow of mice, seeds of higher plants, lysogenic bacteria, microspores of spiderwort, and others. These disorders have a small but statistically reliable value. At the same time, it was established that a combination of flight factors did not cause any persistent and expressed changes in the vital activity of mammals and man. The great practical significance of the biological experiments made on flights before man was launched into space is noted.

In the general research program of studying and mastering the universe, a new area of natural science, space biology, occupies an important place. /67

Some of its principal tasks are the study of the biological effect of factors during a space flight, the development of general biological bases and principles for guaranteeing the safety of space flights, and the examination of the existing conditions and the specific features of forms of extraterrestrial life [50-52].

The problems mentioned above are being studied under the conditions of flight tests in various aircraft and in laboratory experiments using varying testing devices which imitate the effect of certain factors aboard a space flight. It is completely obvious that the two study methods, each with its own advantages and shortcomings, must supplement each other.

It is well known that, in order to conduct biological experiments under flight conditions, we can use high-altitude balloons, geophysical rockets, non-recoverable craft (Earth satellites), and recoverable spacecraft. For biological experiments, the most advantageous seems to be the latter type of aircraft. /68

[1]Report at the IIIrd International Symposium on Bioastronautics and Space Research, San Antonio, USA, November 16-18, 1964.

After an extensive program of biological studies made in high-altitude balloons and geophysical rockets, it became possible to conduct experiments under the conditions of an orbital flight in the Sputniks. At this stage, we could solve many methodological problems and compile new, interesting, data concerning the effect of a number of extreme flight factors on various biological materials: in other words, we could produce the basis for a transition to a new level of studies and experiments in Earth satellites [12, 13, 21, 37, 49].

These experiments began with the historical flight of Layka (1957). Further progress of science and technology has permitted the design spacecraft which can be recovered on the Earth, thus significantly expanding the possibilities for the experimenter. Beginning in 1960, and continuing to this day, Soviet biologists have conducted experiments on 11 recovered spacecraft thus far.

The principal tasks of these experiments were to study the biological effect of combined and individual factors on a space flight, to determine the operational effectiveness of the systems for guaranteeing an organism's life activity, and, finally, to find biological indications for the course of a manned flight [2, 13, 53].

The first problem is examined in this article. It is well known that the factors of a space flight which can show an effect on living organisms can be conditionally divided into three groups:

(a) Those connected with the dynamics of flight in a spacecraft (acceleration, vibrations, noise of the motors, weightlessness);

(b) Those characterizing space as a unique habitation medium (extremely low barometric pressure, changed gas composition with a lack of molecular oxygen, ionizing radiation, etc.);

(c) Those connected with more or less prolonged stay of an organism under the artificial conditions of the spacecraft (limited space, specific features of the microclimate, nourishment, rhythm, etc.) [9, 50, 57].

In the experiments whose principal results are presented in this article, together with the study of the effect of flight conditions as a whole, it also became our goal to study the effect of the least-understood factors, such as weightlessness, space radiation, and their combinations with acceleration, vibration, etc.

Subsequently, in order to eliminate the supplementary effect on an organism of certain factors connected with the artificial conditions aboard the craft (temperature, humidity, gas composition of the atmosphere, etc.), the permissible variations of the principal parameters for the medium in the cabin were reduced as much /69

as possible.

The use of a life-preservation system for these purposes provided for developing and maintaining the given hygienic parameters for the medium in the aircraft's air-tight cabin at the necessary level. The variations of the parameters which did occur were relatively small and did not exceed the permissible limits.

Thus, the barometric pressure in the aircraft's cabin was very close to normal (760 ± 20 mm Hg), the air temperature varied from +11 to +30°, and the relative humidity varied from 30 to 70%. The oxygen content changed from 16 to 29, and the carbon dioxide content changed from 0.2 to 1.2%.

The flights of the spacecraft were made in orbits with similar parameters. The maximum distance of a craft from the Earth's surface (apogee) was 409 km (the "Voskhod" spacecraft). The angle of the orbit to the plane of the equator, in all the flights, was approximately 65°. The flight time varied from 108 min (Sputniks 4 and 5, "Vostok") to 119 hours ("Vostok-5"). Most of the experiments were conducted during the spring-summer period.

The total radiation dose, obtained during the flights, changed from 1.5 mrad (108 min in flight) to 81 mrad (119 hours in flight), respectively, with an average dose from 8.4 to 17 ± 2 mrad/day. We should note that, at these altitudes, with inclination of the orbit at 65°, about 90% of the absorbed dose was caused by primary space radiation, and 10% by emission of the Earth's radiation belts [8, 10, 34, 36, 39, 45].

Let us briefly discuss the principal biological materials used and the ways of studying them.

As a basis for selecting the biological materials, we posited an evolutionary and comparative physiological principle which provided for more comprehensive evaluation of the biological effectiveness of flight factors. The wide spectrum of methods used provided for recording diverse variations in the functions and structures of a cell or of an entire organism.

In these experiments, we used mammals (dogs, guinea pigs, rats, and mice), cultured cells from animals and man, fruit flies (Drosophila), seeds of higher-order plants, microspores of spiderwort, cultures of algae (Chlorella), and multiple microbiological and cytogenetic materials. We used physiological, biochemical, morphological, cytogenetic, genetic, microbiological, and other methods for the studies [3, 20, 46, 54].

As the experiments complicated the tasks to a greater degree, methodical procedures were used. Thus, if the effect of flight conditions was the principal object of study in the experiments on Sputniks 2 to 5, then, for the experiments aboard "Vostok-3",

"Vostok-4", "Vostok-5" and "Voskhod", we attempted to study the effect of individual factors (space radiation, weightlessness, etc.). For this purpose, we expanded the studies by adding radio-sensitive materials (lysogenic bacteria, microspores of spiderwort, and others) and using the genetic changes in the various pharmacochemical media for the analysis. In a number of experiments established mainly for studying the effect of weightlessness on the principal biological processes (reproduction, growth, and development of an organism), we had the participation of astronauts A. Nikolayev, P. Popovich, V. Bykovskiy, and B. Yegorov [4, 22, 24, 43]. Together with these, we continued investigations on the improvement of the automatic bio-elements "AMN" and "BIOS". /70

Corresponding control studies were made under laboratory conditions.

Let us turn to a presentation and discussion of the principal results.

STUDIES ON MAMMALS

In the experiments on dogs (experiments aboard Sputniks 2 to 5), the most attention in the physiological plan was given to a study of the state of the cardiovascular system and respiration. Briefly, the results obtained can be presented in the following way.

During the flight segment when the satellites entered orbit, the reactions of the cardiovascular system and the respiration in the majority of the animals were uniform and clearly expressed. The character of their reactions reflected the state of the functional stress for these systems: the rate of heart contractions increased, respiratory motions became more frequent, and the blood pressure increased.

In the state of weightlessness, which was maintained for as long as one day during the experiments aboard the second and third satellites, the recorded characteristics returned to their original, pre-launch level. However, the phenomenon of "retention", a slower normalization (in comparison with control experiments in a centrifuge) of the functional characteristics for the cardiovascular system and for respiration, was also noted here.

Moreover, there frequently appeared an instability in the rhythm of the heart contractions, variations in the numerical indices of the electrocardiogram (R-R interval, value of the T wave), and a relative decrease of the systolic characteristic. All this indicates, to a certain extent, that there are certain unique features in the dynamics of regulating the vegetative functions under the conditions of weightlessness [7, 13].

In the experiments on the satellites, we also attempted to

study the character of kinetic activity for dogs under conditions of weightlessness. The animals were capable (within certain limits) of free movement. The development of the televised and telemetric data showed that there was a clear tendency to automatize frequently-repeated motions (for example, motions directed toward fixing the body in space) [33].

An analysis of the forces developed by the animals in the state /71
of weightlessness showed that by repeating exercises up to several hundred times, the animal could perform this task with minimum energy expenditure. It is interesting to note that, for guinea pigs, the electrocardiograms for the posterior extremities showed increased impulsion for the first ten days after returning from a flight. However, in the control animals, the change in the bio-electric activity of muscles was observed in a weak form, and only during the first day after returning to the laboratory [38].

The condition of higher nervous activity was studied in experiments with rats. The motor-alimentary method did not show any changes in the length of the latent period or in the amount of reflexes. The data obtained indicate that the functional changes in the central nervous system are obviously limited by the sphere of the motor apparatus [13, 38].

Biochemical studies on the blood and urine of dogs who were subjected to a 24-hour flight on Sputnik-2 showed a transitional and moderately-expressed stress reaction which was characterized by a short-period increase in the α_2-globulins and the serum mucoids. However, we did not succeed in finding any changes [19] in the dogs who had undergone one-revolution flights on Sputniks 4 and 5.

In a number of experiments (on Sputniks 4 and 5), we examined the content of serotonin (oxytryptamine-5) in the blood of dogs and mice. It was established that, the flight causes a decrease in the level of amine in the animals' blood, with subsequent normalization a short time after landing [41].

In examining natural immunity in dogs (quantity of microbes on the surface of the epidermis, bactericidal properties of the blood) after flights aboard space probes, we noted variations in immunological reactivity, with predominance of the activation phases. These shifts returned to their original level rather rapidly (during the first week after the landing) [1].

The control experiments conducted under laboratory conditions showed that the changes in the functional state of the cardiovascular and other systems and certain variations in the metabolic processes found in animals affected by a space flight, can also occur because of individual flight factors - vibration, acceleration, as well as combinations of these [11, 19, 35, 41].

Thus, having analyzed the results of the physiological studies

conducted during and after the flight, as well as the biochemical studies conducted a short time after the flight (during the first week after the landing), and having compared them with data from later observations, we see that the recorded changes reflected a stress reaction caused by the effect of a combination of flight factors. /72

We will discuss briefly the results of cytogenetic studies on the bone marrow and spleen of mice who were aboard Sputniks 2, 4, and 5. It was shown in these experiments that the flight caused the percentage of chromosome rearrangements and adhesions of the chromosomes in the cell nuclei of these organs to increase with statistical reliability [5, 6]. In a pathomorphological examination of the parenchymatous organs, dystrophic, mostly reversible, changes were found. Control experiments under laboratory conditions showed that such changes do occur in mice, not only because of the effect of ionizing radiation (as was previously known), but also due to the effect of vibration and acceleration [5, 6].

STUDIES ON A CULTURE OF CELLS OF THE "*HELA*" STRAIN

This material was used in experiments on Sputniks 2, 4, and 5, and on "Vostok-4" "Vostok-5", and "Voskhod". For various reasons, this strain proved to be the most advantageous for similar experiments. We studied the effect of a combination of flight factors on the viability of the cells, the character of their growth, and their antigenic and morphological properties. We provided for a study of the possible integration of the effect of factors in a space flight, using one culture repeatedly in a number of experiments (on "Vostok-4", "Vostok-6", and "Voskhod").

The studies made with a culture of the "Hela" cells show that the viability of the culture was preserved under these conditions. Only certain immunobiological changes were noted in the cells, which were not linked with the length of the flight and obviously were caused by a non-specific effect of extremal factors [28-30].

We can consider that in the process of conducting flight tests there can be a selection of a certain type of cells which are adapted to preservation under disadvantageous conditions of experiments and controls. Subsequently, the lines of cultures with cells of the Hela strain thus selected are very valuable materials for studying the effect of longer flights and higher levels of space radiation on human cells.

EXPERIMENTS WITH *DROSOPHILA MELANOGASTER*

First, let us examine the results of experiments conducted on Sputniks 2, 4, and 5 and "Vostok-1", "Vostok-2", "Vostok-3", and "Vostok-4". In the experiments, we used flies of different lines. The effect of the factors (principally, space radiation) on these materials was estimated on the basis of their effect on the

rate of occurrence of sex-linked dominant and recessive lethal mutations and their effect on the rate of occurrence of primary non-divergence for the X-chromosomes. An analysis of the data obtained shows primarily, that there is no clear relationship between the genetic changes in *Drosophila melanogaster* and the length of the flight. Thus, having examined the effect of space-flight factors '73
on the rate of occurrence of sex-linked recessive lethal mutations, we can see that statistically reliable changes were found for the flights on Sputniks 2 and 4 and "Vostok-1", while none were discovered for the flights of Sputnik 5 and "Vostok-2". There was also no mutagenic effect found in the experiments with fruit flies (Drosophila) for the flights of the "Vostok-3" and "Vostok-4". The statistically reliable effect for dominant lethals was found in the experiments on Sputniks 2 and 4; in the experiments on "Vostok-2", "Vostok-3", and "Vostok-4", the effect was statistically unreliable. The effect on the rate of occurrence of a primary non-divergence of the X-chromosomes s studied aboard "Vostok-1","Vostok-2", and "Vostok-3". Then, in the experiments on "Vostok-1" and "Vostok-2", the genetic effect was statistically reliable, while this was entirely lacking in the experiment on "Vostok-3" [14, 15, 17, 27, 42, 44].

Unfortunately, for reasons not connected with the effect of space-flight factors, the experiment with Drosophila aboard "Vostok-5" and "Vostok-6" could not be completed. All the flies died after landing - probably as a result of unfavorable temperature conditions.

The program of biological studies aboard the "Voskhod" also entailed conducting experiments with *Drosophila melanogaster*. The experiments were performed on flies of two lines: "white" and "Domodedovo-32". A significant place in these examinations was given to the study of the protective effect of methoxytryptamine-5, an active anti-radiation medium. The experiment is still not complete, and it is therefore difficult to discuss its scientific significance at present. However, we should note that the materials arrived in the laboratory in good condition and the experiment was conducted successfully.

How can we explain the appearance in some flights and the lack in other flights, of hereditary changes in fruit flies (Drosophila)? We might think that the genetic effect was caused by vibration and acceleration. However, if this effect depended on these factors, their mutagenic action should occur for all seven flights. The hereditary changes in fruit flies (Drosophila) are probably not linked to the effect of weightlessness either, since there was no relationship in the experiments between the appearance of the effect and the increase in the time of weightlessness. We have not excluded the idea that an important role in the occurrence of genetic effects for Drosophila during flight can be assigned to hard cosmic radiation. It is completely obvious that this assumption requires further experimental proofs obtained in laboratory experiments, for explaining the combined effect on the hereditary struc-

tures of vibration, acceleration, and ionizing radiation, and obtained in flight tests which continue for a long period of time.

We have reasons to hope that the application of methoxytryptamine-5 (an experiment aboard the "Voskhod") will greatly aid in establishing the cause of the genetic effects discovered in certain flights. /74

Let us discuss the results of an experiment conducted with the aid of the astronauts Nikolayev and Popovich. The principal goal of this experiment was to study the reproduction processes in *Drosophila melanogaster* in the state of weightlessness. Males and females of the wild laboratory line "Domodedovo-32" were used.

The progeny developed from eggs which were laid under the conditions of weightlessness and immediately after landing were studied in the laboratory. In order to analyze and evaluate the imposed disorders, we calculated the speed of embryonic development, the quantity, sex, and weight of the flies being hatched, the divergence from the norm for the shape of the body, the size, color, and shape of the eyes, and the size and venation of the wings. The mature sperm of the males which were hatched were analyzed for the presence of lethal and visible recessive mutations in the genital chromosome.

An analysis of the experimental data showed that fertilization, laying of the eggs, and development of Drosophila can occur normally under the conditions of weightlessness for up to 4 days. In these experiments, we found an abnormality in the sex ratios: in all the cultures, the number of females significantly exceeded the number of males, whose hatching occurred somewhat later [43].

The excess in the number of hatched females over the number of males can be explained in a number of ways. One is the selective effect of space flight on sperm with Y-chromosomes, complicating their utilization. Moreover, the abnormality of the sex ratio among flies which were hatched later could be caused by the loss of Y-chromosomes in meiosis. However, it is more probable that, under experimental conditions, the survival-capacity for the male larvae was lowered, or the survival-capacity for the female larvae was increased.

Having emphasized our great interest in the data obtained in this experiment, we should note that they have only qualitative significance, and they do not permit a quantitative calculation of the changes in the mating energy, the life capacity of the embryos and larvae, etc. These characteristics could change in relation to the geotropism of Drosophila, but in order to find them we would probably have to determine the variations in the corresponding characteristics in the plus-minus lines selected by this index. Moreover, in conducting quantitative examinations, we could never produce an overpopulation in cultures, as was done in these experi-

ments, because this conceals the change in reproduction energy and prevents a precise calculation of the effect of flight factors on the life capacity of an organism, etc.

We should also note that in analyzing the experimental data, /75 we did not find any substantial effect of flight conditions on the shape-development of the flies. The recorded decrease in the sizes of the species can be completely explained by their development in a more compact trophic medium and under the conditions of overpopulation. Although the percentage (0.83%) of discovered anomalies in their development is very high, and we must consider the possibility of preferred elimination of anomalous varieties in this case, their character is nevertheless not specific and their absolute number is small.

The question on whether or not factors of space flight have an effect on the shape-development, and which factors these are, should be the subject of further study. In all probability, the average values for the characteristics determined in the development of variations under the conditions of weightlessness can be shifted to one side or the other. The total variance, reflecting the accuracy in channeling the development to various conditions of the exterior medium, also changes, as does the individual variance, determined by the stochastic variability of the development. In particular, the study of the phenotype appearance of mutations involving the structure of the wings is of great interest in the development of variations under the conditions of weightlessness. The novel conditions of the medium, with lack of a phylogenetic basis for such mutations, can cause formation of shapes which differ sharply from those developed under normal conditions [4, 43].

STUDIES WITH PLANT MATERIALS

In the experiments, we used Chlorella, dry seeds from higher plants, and microspores of spiderwort.

Various strains of Chlorella were exposed on Sputniks 2, 4, and 5, and on "Vostok-5", "Vostok-6" and "Voskhod". These strains differed in shape, cell size, ability to give off oxygen, resistance to radiation, etc.: in the experiments, we used various trophic media. We studied the effect of a combination of flight factors on the life capacity and mutability of chlorella. The dynamics of the development of the Chlorella cells and their survival was studied by the method of calculating microcolonies. The method for calculating macrocolonies was used for determining mutations.

An analysis of the experimental data shows that there is no significant effect of flight conditions on the survival and rate of mutations for most of the Chlorella strains examined. At the same time, for those which were least resistant to radiation, there was a definite tendency to a decrease in survival and an increase in

mutability. However, the difference in the mutability relationship did not seem to be statistically reliable, and the decrease in survival was small and insignificant for an intensive culture [20, 47, 52].

The experiments with dry seeds from higher plants were conducted on all the craft. The seeds of wheat, onion, tomatoes, /76
pines, beans, spindle trees, and others were used for the physiological and cytogenetic studies examined in this article.

The physiological studies provided for determining the absolute germinating capacity of the seeds and for studying the course of germination and the development of roots.

These experiments showed that a combination of flight factors has a varying effect on the inability of the seeds in the majority of the types of plants studied, causing stimulation in some cases and suppression of germination in others. In a quantitative relationship, these changes are small and, as a rule, unreliable. In a number of cases, there was no flight effect found [18, 48, 52].

The cytogenetic studies examined the chromosome rearrangements in the first mitoses of the roots' primary rootlets.

An analysis of the data obtained showed that the flight caused the percentage of chromosome rearrangements in most of the seeds being studied to increase. However, this increase was statistically reliable only for certain seeds: wheat, peas [16, 55, 56], carrots, and tomatoes [25]. There were more chromosome rearrangements in the experimental samples and more chromatin rearrangements in the controls. Moreover, there were more recombinations in the experiment and more fragments in the control.

We should note that there was no correlation among the amount of chromosome disorders, the radio-sensitivity of the seeds, and the length of the flight. Thus, for example, the percentage of chromosome rearrangements in radio-sensitive pine seeds was much lower than in radiation-resistant onion seeds (experiments on "Vostok-5" and "Vostok-6". The degree of the effect for most of the seeds being studied did not depend on the length of the experiment, and the genetic injuries obtained as a result of one-, three-, and five- day flights were, as a rule, identical in value [25, 52].

The experiment with spindle-tree seeds, conducted during the flight of the "Vostok-5", is of certain interest. During this flight, the seeds were planted in both the intact and irradiated states (10,000 rad). It was found that flight conditions in both cases caused an increase in the yield of cells with chromosome aberrations (3% on the average). In the case of irradiation, there was integration of the effect of ionizing radiation acting on the Earth and the flight conditions [40].

How can we explain the physiological changes and the genetic disorders appearing in the dry seeds of higher plants affected by space flight? Stimulation and oppression of growth and an increase in the percentage of chromosome rearrangements were found in dry seeds of various types in all the flight experiments. The lack of a relationship between the observed effects and the length of the flight as far as radiation sensitivity is concerned gives us a basis /77 for assuming that the physiological changes and the chromosome disorders are probably not linked with the effect of weightlessness and space radiation, but are caused by a complex effect of mechanical factors during launching and landing. At the same time, the results obtained for the flight experiments do not allow us to exclude the idea of the participation of hard cosmic rays in the genetic effects. It is obvious that in order to explain the reasons for these phenomena we must conduct special experiments under flight and laboratory conditions, which will allow differentiating the effects of individual factors. It seems to us that these problems can be solved principally in experiments with roots, which must be performed during different orbits of a flight, and also in experiments using media which are resistant to various flight factors.

Microspores of *Tradescantia paludosa* were widely used for cytogenetical studies, beginning with the experiments on "Vostok-3" and "Vostok-4". Astronauts Popovich, Bykovskiy, and Yegorov participated actively in the experiments with these materials. They performed experiments with some of the materials, 1½, 23, 56, 76, and 120 hours after the craft entered orbit, thus obtaining interesting data for differentiating the effects of vibration and acceleration occurring during launching and landing, from the effects of weightlessness and space radiation.

A cytological analysis of the microspores of Tradescantia revealed three types of changes occurring as a result of the flight: (a) rearrangements of the chromosomes; (b) disorders in mitosis mechanisms; (c) disorders in growth processes.

The flight conditions for all four "Vostok" craft caused a great increase in the number of chromosome rearrangements. Thus, the total percentage of rearrangements in the metaphase and anaphase during the experiment on "Vostok-3" was 1.89 ± 0.08; for "Vostok-4", "Vostok-5", and "Vostok-6", it was 1.49 ± 0.04, 1.24 ± 0.10, and 1.94 ± 0.09, respectively. Analysis of the data from the "Voskhod" has not yet been completed: however, the previous results give us reason to hope that the facts obtained will be a substantial supplement to the data we now have.

We should note that, among the chromosome disorders we found, a new type of rearrangements played a significant role: spherical fragments which were recorded, not only in the metaphase, anaphase, and telophase, but also in the prophase and interphase. In the laboratory experiments, this type of rearrangement was found only under the influence of high acceleration (4000 g and more).

A question naturally arises: which flight factors cause the chromosome disorders in the Tradescantia microspores? An analysis of the data, obtained with the aid of Bykovskiy, indicates that various types of chromosome rearrangements are probably caused, /78 mainly, by the effect of factors linked with launching and landing. The greatest percent of disorders was recorded during the first hours after the craft entered orbit, and the least was recorded before landing. After landing, the number of rearrangements again increased.

In addition to the chromosome rearrangements, disorders were also found in the mitosis mechanism. The principal disorders were the non-separation of chromosome complexes, the remaining of individual non-separated chromosomes, three- and four- polar mitoses, and a change in the direction of the spindle axis.

As the studies showed, the total percentage of disorders in the mitosis mechanism was definitely linked to the length of the flight. Thus, for example, during the experiment on "Vostok-5", when the materials were in a state of weightlessness for 1.5 hours, the total percentage of cells with mitosis disorders was 0.49, while during the 119-hour flight it was 7 times greater (3.1). Therefore, this and other facts indicate that the disorders in the mitosis mechanism were certainly linked with the effect of weightlessness [4, 22, 23, 24].

We should briefly mention the disorders in the growth processes in individual cells of Tradescantia microspores which were subjected to flights on "Vostok-3" and "Vostok-6". The experimental data showed that there was formation of protuberances in the cells, giant cells, and certain disorders in the synchronism of microspore development in the anthers.

EXAMINATIONS WITH LYSOGENIC BACTERIA *E. COLI* K-12 (λ)

These materials were used on Sputniks 4 and 5, "Vostok-1" to "Vostok-6" and "Voskhod". The injurious effect of flight factors, primarily space radiation, and also the resistant "antigenetic" effect of mercaptopropylamine-β (experiments on "Vostok-5" and "Vostok-6", and "Voskhod") and methoxytryptamine-5 (experiments on "Voskhod") were calculated by inducing phage-production in the experimental and control samples.

These experiments showed that a combination of flight factors causes an increase in the degree of phage-particle production for the lysogenic culture *E. coli* K-12 (λ). This effect was found very clearly in the experiments, beginning with "Vostok-3".

In analyzing the experimental data obtained in all the flights, we can see the lack of a clear dependence between the amount of induced phage-production and the length of the flight. As we know, this circumstance was also found in the experiments with dry seeds.

An examination of the resistant properties of mercaptopropylamine showed that this preparation, although it lowers the level of phage-producing activity for *E. coli* K-12 (λ), and has a genetic effect (affecting the genetic structures), it nevertheless does not protect the bacteria from the lethal effect of space-flight factors [31, 32]. The data on the study of the protective properties of methoxytryptamine-5 should be of definite interest: it differs from mercaptopropylamine-β in its effective mechanism. /79

How can we explain the inducing genetic effect we are examining, which was found in lysogenic bacteria during experiments aboard spacecraft? It is well known that lysogenic bacteria are sensitive to radiation, and react to the effect of relatively small doses of ionizing radiation (200-400 mrad). This reaction is observed during the action of various types of ionizing radiation: x-rays and γ-rays, fast neutrons, and high-energy protons [31]. However, it does not follow from this that the induction of *E. coli* K-12 (λ) in the experiments on the spacecraft was connected with the effect of only one type of space irradiation in small doses. We have more reason to assume that this effect is caused by the combined action of vibration, acceleration, weightlessness, and ionizing radiation. The possibility that the dynamic flight factors sensitize the lysogenic culture in conjunction with the effect of space radiation (which is also the reason for the induction of bacteria at small doses) is not excluded. This assumption is substantiated by laboratory investigations, in which it has been seen that vibrations can greatly increase the sensitivity of *E. coli* K-12 (λ) to the effect of ionizing radiation [32].

Thus, we have examined and analyzed the principal results of the airborne biological experiments conducted on Sputniks 2 to 5 and "Vostok-1" to "Vostok-6".

On the basis of the experiments conducted on Sputniks 2 to 5, we have drawn a conclusion which has great practical significance: space flight does not have a disadvantageous biological effect on animal organisms. In fact, the "permit" for the first manned orbital flight was granted on the basis of these data. It is very obvious that this conclusion should be considered as valid only for concrete conditions in the experiments conducted, from the point of view of the flight duration, the altitude, and other orbital parameters.

The completion of the outlined program for the biological examinations provided for obtaining new data characterizing the factors of space flight, and space as a source of harmful hereditary changes for a number of biological materials. The first attempts have been made to solve the exceptionally interesting and practically important problem of protecting the hereditary structures from the injurious effect of a combination of flight factors, with the aid of pharmacochemical media.

We can see from these data that this is the beginning of a study on the biological effect of space-flight factors, the first steps in examining weightlessness, space radiation, and the effect of a combination of flight factors. The results of the biological experiments on the spacecraft showed that a state of weightlessness, /80 continued for five days, is not reflected negatively in the life activity of various organisms. Moreover, the manned flights on these craft showed that man's coordination and orientation in space do not suffer under conditions of weightlessness. However, these experiments do not answer the question of whether or not a long period spent in a state of weightlessness can change the functional state of an organism to such a degree that return to the conditions of a normal gravitational field (for man) constitutes an acceleration.

Moreover, we must consider that the Earth's gravitational field obviously has a definite effect on the physiology of cellular and subcellular structures, on the shape-development, and on embryogenesis. A number of factors obtained in the flight experiments indicate that the state of weightlessness can cause certain disorders in the mechanism of mitosis. Subsequently, we can consider that a long absence from the effect of the force of gravity can change these processes substantially, causing disorders in the balance of the ecological system. If these assumptions are confirmed, it will be necessary to solve the problem of the elimination of weightlessness by producing artificial gravity in the craft. To what degree this is necessary, and what values of artificial gravity should be recommended for man and various representatives of the ecological system: all this requires an experimental solution.

Solution of radiobiological problems has exceptional significance. Some of the principal problems are: examining the relative biological effectiveness of individual components, studying the genetic effects of radiation, examining the combined effect of ionizing radiation and other flight factors on an organism, and developing ways to ensure the safety of the crew members and the entire bio-complex of the craft.

It is quite obvious that in order to answer these questions, and in order to solve the essential biological problems which have important significance for the use of future space flights, we must collect and analyze more experimental facts. In this case, we should keep in mind that the biological studies should be designed with possibly more complete consideration of the physical features for a unique medium (space) and that the progress of physical studies in space is an important prerequisite for the successful development of the principal trends in space biology.

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ELECTROENCEPHALOGRAPHIC STUDIES IN SPACE MEDICINE

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ABSTRACT: The electroencephalographic method (EEG) is examined in relation to the tasks of space medicine. It is shown that the EEG can be used successfully for selecting astronauts, in the system of medical control during the preflight preparation period, and during space flight. The EEG provides an objective determination of an astronaut's level of sleep and wakefulness, and the state of his working capacity.

It has already been said often enough in the literature that, /83
just as an analysis of the problems of communication and control became an important problem during the energetic development of XIXth-century technology, the center of interest for studies in physiology is also gradually moving toward an analysis of the informational and control processes. Such a shift in interest not only provides for developing this difficult but extremely important area of physiology, but also has shown a substantial effect on the development of traditional areas in physiology. One proof of such an effect can be seen in the fact that physiologists are concentrating more and more on the complex study of an organism in all the forms and appearances of its life activity, which are found in its active interaction with the surrounding medium and in its active reaction to events of the world around it.

The activity states of a human organism became of great interest mainly after the First World War, and this interest was marked by the development of a new area in physiology: the physiology of labor, and, in particular, of aviational labor. The beginning studies in this area nevertheless showed traces of the preceding stage, with predominant attention to the problems of energy and metabolism.

The progress of science and technology, and the change in the character of human labor activity, particularly in the range of special types of labor, reconfirm the value of a complex study of man in the process of various types of his activity. This is particularly apparent in relation to the studies concerning the conquest of outer space.

In this article, we will concentrate on the practical aspects of using the electroencephalograph (EEG) for evaluating the functional state of an astronaut's central nervous system. We will be

speaking about varying situations in which an astronaut finds himself, both in the process of preparing for a flight, and under conditions of space flight. The use of electroencephalography, under the conditions of space flight and also during an imitation of various factors on the Earth, forces us to diverge from the traditional clinical and physiological methods for EEG studies, for which an artificial sensory exhaustion is characteristic (produced by a decrease in exposure, sound insulation, and by a passive position during the observation time). Therefore, it is essential that the characteristics of normal electroencephalograms and their classification should be examined in relation to new study conditions.

Thus, for example, in the process of selecting subjects, we /84
can examine their pronounced orientation reaction when they are in a circumstance which is unusual for them. The dynamics of this reaction can be recorded objectively by the depression of the α-rhythm and its recovery. This test in itself has expert value, since it characterizes the functional state of the central nervous system, and principally the emotional reactivity of the subject.

For a more complete characteristic of the orientating reaction, we can use various external stimuli (light, sound, etc.). In this examination, we can find those whose orientating reaction does not die out for a long period of time; this is obviously an objective indication of emotional instability.

After the orientating reaction dies out, a stable EEG picture, is usually established, which characteristic for the given individual and can be evaluated qualitatively (on the basis of generally-accepted criteria) as well as quantitatively.

A quantitative analysis of the EEG, with the aid of spectrum analyzers and integrators, shows that, for one and the same subject under various conditions, the energy distribution in various parts of the EEG spectrum is relatively constant, and varies by 10-15% in all. On the basis of this, we can assume that the EEG is an important element of man's physiological characteristics, and can be used in combination with other indicators to determine the changes in the subject's behavior under various flight conditions.

During the EEG tests, hyperventilation, hypoxia, vibration, as well as angular and radial acceleration are usually applied simultaneously by functional flights.

Hyperventilation makes it possible to find those subjects who, during low hypocapnia (when the partial pressure of carbon dioxide in the alveolar air is still relatively high - 28-30 mm Hg), show a definite dominance of slow oscillations with high amplitude in the EEG, along with simultaneous disorders corresponding to the activity of the central nervous system (hypocapnic spasms, eye troubles such as blurred vision and black-out, and loss of consciousness). In individual cases, there are observed exophthalmus,

sharp dyspnea, disorders in the nervous activity, etc. Thus, we can find those subjects whose EEG has a normal background, but who are unusually sensitive to hypocapnia.

Changes in the bioelectric activity of the brain during severe oxygen deficiency were studied in more detail. The studies of Davis, Davis and Thompson, Gibbs, Gibbs and Lenox, Shtrukhgol'd, Baygel, Palme and Harshtik, Shchpil'berg, Malkin, and others showed that, /85 with development of severe hypoxemic hypoxia, there are orbit changes in the EEG which reflect the degree of the hypoxic condition. In this case, there are usually 3 or 4 orbits: an orbit with activation of high-rate vibrations (β-rhythm) coinciding in time with a development of compensator reactions on the part of the cardiovascular and respiratory systems; an orbit with activation of the α-rhythm, which also occurs even against a background of relatively low working capacity; and an orbit with predominance of slow oscillations in the EEG, having two stages: appearance or increase of single and short groups of 5- to 7-Hz vibrations of increased amplitude, accompanied by the appearance of the first clinically-expressed warnings of a lowering of the working capacity (disorganization in the handwriting, increase in the latent periods of motor reactions, lowering of the intellectual level, etc.), and a second stage with predominance of waves of the Δ-rhythm with high amplitude, with simultaneous appearance of a practically complete loss in the working capacity and the appearance of gross disorders in the nervous activity (clonic spasms in the muscles of the writing hand, loss of the ability to write, and varying degrees of consciousness, including complete loss of consciousness). The picture of the changes in the EEG given above is typical for the development of the so-called altitude syncope.

However, as the studies conducted at relatively low altitudes (5000-6000 m) on healthy average subjects during the development of a hypoxic state, there can be a decrease in the voltage of the bioelectric potentials, with predominance in some cases of low-voltage, high-rate vibrations, i.e. there is a pronounced desynchronization, probably caused by an increase in the excitability of the trunk structures (reticular formation). In this case, the clinical picture of the hypoxic state for the examinees develops with clear appearances of trunk symptomatology: hyperhydrosis, sharp changes in the blood-circulation for vessels in the face, bradycardia, nausea, and sometimes vomiting. We should mention that, against the background of a pronounced decrease in the voltage of the biological currents, a retardation and shift of the posture is developed; the latent periods of arbitrary motor reactions increase, i.e. a picture of retardation is developed, which many researchers link with an intensification of slow oscillations in the EEG. In cases when the condition of the subjects continues to worsen, they rapidly lose an active position.

Thus, for a lowered resistance to hypoxia, there are two different pictures of changes in the EEG obviously linked with

different mechanisms for the effect of oxygen deficiency on the central nervous system. In the first case, with a gradual and increasing shift in the EEG toward low rates, and the clear appearance of a predominant slow rhythm, the oxygen deficiency has primarily an oppressing effect on the cerebral cortex. In this /86
case, regulation of the vegetative functions is fixed for a long period of time. In the second case, the effect of hypoxia dominates over the reticular formation of the trunk and the mid-brain; in this connection, there are pronounced vegetative disorders, and signs of desynchronization (caused by the activating effect of the reticular formation on the cortex) in the EEG for a long period of time. We should keep in mind that many exogenic factors, causing the subject's stress reaction while the hypoxia test is being conducted, can produce such a character in the reactions. Therefore, a definitely negative judgement should be given only for those cases when the decreased resistance to hypoxia occurs in a situation which completely excludes a previous effect of substantial value for the stress-factors, or in those cases when repeated examinations show decreased resistance each time.

Thus, EEG studies using hypoxic and hypocapnic tests can have substantial value for definite evaluation in selecting astronauts and in their training.

It is well known that astronauts are subjected to effects of various types of mechanical energy during training: increased gravitation (in training on centrifuges), and vibrations on special vibration-stands. They are also subjected to the effect of angular accelerations which have varying direction. In these cases, the EEG plays a substantial role in the examinations. This is caused by the fact that the evaluation of the functional state for the central nervous system during the events mentioned above is based to a large degree on the data of the EEG. The EEG data can be used in two ways: on one hand, as an indicator of the subject's resistance to one or another functional stress, and his ability to adapt to it during the training process; on the other hand, the accurate representation of the reactions of the brain's bioelectric activity to the isolated effect of separate dynamic flight factors permits pinpointing the changes which are linked with certain factors under the conditions of a real flight, by a suitable comparison of data. Hence, it is of great interest to examine the dynamics of the changes in the subject's bioelectric brain activity during the effect of radial accelerations directed perpendicular to the lengthwise axis of the subject's body. The studies of A.R. Kotovskaya, P.M. Suvorov et al., A.S. Barer, and others have shown that transverse accelerations cause regular changes in the brain's /87
bioelectric activity, which can be divided conditionally into three orbits. In the first orbit, the character of the EEG does not change substantially, and there is only a certain intensification of the β-rhythm with a weakening of the clarity of the α-rhythm. As the acceleration increases, this orbit turns into the next: there is activation of the α-rhythm, which becomes pronounced, not

only when the eyes are closed, but also when they are open.

In the third orbit, there is a weakening of the α- and β-rhythm, and slow oscillations with a high amplitude gradually begin to dominate the EEG. In this case, when the action of the accelerations is continued, many examinees had eye troubles (blurred vision and black-out), and there were even greater changes in the activity of the central nervous system. It is important to note that the changes in the EEG during acceleration at a certain intensity are not identical for various people, and they largely agree with the examinee's individual resistance. Thus, the EEG is one objective criterion for determining a person's endurance to radial accelerations.

It is remarkable that the above-mentioned orbits for the changes in the brain's bioelectric activity during the effect of transverse accelerations essentially coincide with the dynamics of the changes in the EEG during the effect of accelerations which have the direction, "head-pelvis". The only difference is that the second and third orbits for the changes in the bioelectric activity during the effect of transverse accelerations occur at greater stress values than during acceleration in the direction, "head-pelvis".

Along with the effect of general vertical vibrations, there are also definite changes in the EEG which depend on the rate and amplitude parameters of the vibration as well as on the length of its action. Thus, according to the data of I. Ya. Borshchevskiy, , M.D. Yemel'yanov, A.A. Koreshkov, V.G. Terent'yev, and others, for the action of vibrations with a rate of 10-40 Hz in the cases when the amplitude does not reach 1 mm, there are no significant changes noted in the EEG; only when the time of the effect is increased up to 3-4 hours can we observe a clear activation of the β-rhythm and a weakening of the α-rhythm.

For the effect of vibrations with a rate of 10-40 Hz and amplitudes of 1.6 mm, 50 Hz and 1.2 mm, 60 Hz and 0.8 mm, 70 Hz and 0.6 mm, and particularly for the effect of a vibration with a rate of 10 Hz and an amplitude of 2 mm and more, there are orbit changes in the EEG which are similar to the changes described above for the action of transverse stresses of high value; i.e. after the first orbit - activation of the β-rhythm - the slow oscillations gradually begin to prevail on the EEG, and retardation appears more sharply /88
in the conduct of the subject.

In comparing the results of the electroencephalographic studies, obtained during the action of various factors (severe oxygen deficiency, stress, vibration, etc.) on the human organism, there is noted a definite similarity in the changes. It is remarkable that these general EEG changes, characteristic of the effect of various factors, are so clear that it is much easier to discover them than to find specific changes occurring as the result of

definite stimuli. We should also note here that the separate orbits of the general changes are expressed differently for the isolated effect of factors. Thus, for example, in the case of pronounced hypoxia, the orbit with activation of the beta-rhythm is either repeated or, in some cases, is not found; while, in the action of acceleration and vibration of rather low value, this orbit is dominant.

As we have already noted, the specific changes as a result of a certain factor (acceleration, hypoxia, etc.) as a rule are found with much more difficulty, which probably depends somewhat on the study method. We have reasons to assume that an increase in the number of monopolar intervals, and the use of various stimuli (sound, light, etc.) for obtaining the potentials imposed, in combination with the coherent method of EEG analysis, provide for greatly expanding our knowledge on the specific change in the EEG for a definite type of effect.

Studies in which the mechanism of the orbit changes in the EEG has been examined are of particular interest. At the present time, we know of three principal methods for experimental examination.

(1) A simultaneous recording of the bioelectric activity for the cortex and the subcortical formations, along with a determination of the sequence for the development of the changes in various anatomical structures and their comparison with the motor and vegetative changes and the development of certain forms of disorders in the activity of the central nervous system.

(2) A determination of the value for the intercentral relationships, involving studies in which the removal or isolation of individual structures of the cerebrum is achieved by cutting the cerebrum at different levels.

(3) Studies in which attempts are made to compare the activity of certain formations in the central nervous system with the activity of separate cellular elements which comprise these formations.

In the studies in which, during the effect of accelerations and hypoxia on animals, there was simultaneous recording of the EEG for the motor cortex of the cerebrum, hippocampus, reticular formation of the mid-brain, and hypothalamus, it was discovered /89
that orbit changes exist for all the above-mentioned formations. In this case, it was shown that, during acceleration, the changes in the electric activity of the reticular formation in a number of cases somewhat precede similar changes in other regions of the brain.

Some unexpected results (from a theoretical point of view) were obtained in experiments with animals developing severe hypoxic conditions which led to complete elimination of the bioelectric

activity for the cortex, the reticular formation of the brain, the mid-brain, and the hypothalmus.

During the development of serious hypoxic conditions, in the cases of spontaneous recovery of respiration, it was discovered that the recovery of the bioelectric activity for the brain, as a rule, begins with the cerebral cortex, after which recovery begins in the hippocampus and subcortical formations (V.B. Malkin, G.V. Izosimov, A.N. Razumeyev).

These results are of interest in that they are in definite opposition to the general concepts developed by Jackson et al., L.A. Orbeli, V.V. Strel'tsov, and others, who maintain that the mechanisms of the effect of hypoxia and certain other factors on the central nervous system is based on a laminar disconnection of the cerebral structures, running from top to bottom.

The results of studies in which the cerebrum was cut at varying levels and the most important introceptive reflexogenic zones were disconnected, provide a definite concept of the mechanism of the formation of orbit changes in the EEG. The studies of Dale and Bonval established that the denervation of the sinocarotid region, like the anatomical separation of the reticular formation from the cerebral cortex, results in eleimination of the first phase (activation of the β-rhythm during the development of a hypoxic condition in an animal). This gave us a basis on which we could assume that the first orbit is caused by stimulation of the cerebral cortex through the reticular formation, whose functional condition is changed mainly in relation to the appearance of the corresponding afferentation. The data presented above were confirmed in studies by Soviet researchers; in this case, it was found in examining isolated stria of the cerebral cortex that, despite the elimination of the usual intercentral relationships in the early orbit of hypoxia, in which there is activation of the β-rhythm in the intact hemisphere, the isolated stria show an increase in the number and amplitude of discharges simultaneously with a decrease in the limit for a direct evocation of a cortical response during an electrical discharge. These data indicate that during the first orbit of the changes in the EEG, there is already an integrated action for hypoxia of the cerebral cortex: activation through the reticular formation and a direct humoral stimulating effect (V.B. Malkin, N.M. Asyamolova, et al.). /90

The simultaneous examinations of individual neurons and of the integrated bioelectric activity are very helpful in studying the mechanism of the changes which determine the picture of the phase changes in the EEG. In this way, the well-known studies of Jaspar and Lee and Kraytsberg et al. are of great interest. They maintain that, during the process of the development of a hypoxic condition, there is an increase in the frequency of impulse activity for the cortical neurons in the beginning, and then a gradual depression of their activity. In many cases, this can be stopped completely, and

it sometimes does not occur even after an animal is made to breathe pure oxygen. Naturally, the period for activation of the cortical neurons in the initial orbit of the development of hypoxic conditions coincides in time with the appearance of activation for the β-rhythm on the EEG, which, obviously, could be a good reason for concluding that there is a natural increase in the excitability of the cortical neurons during this orbit. At the same time, the oppression of the activity for the neurons during the period of the development of slow oscillations on the EEG indicates that this orbit is caused by a definite decrease in the activity of the cortical neurons. The studies mentioned above were conducted mainly on a model such as hypoxia. However, the fact that the orbit changes in the EEG are not strictly specific for hypoxia gives us the basis on which we can assume that the changes in the EEG occurring for other effects (stress, vibration, etc.) have similar mechanisms.

Actually, as the studies by O.G. Gazenko, B.B. Yegorov, and A.N. Limanskiy show, by the effect of accelerations, there is noted at first an increase in the impulse activity for the neurons of the reticular formation of the brain stem. In this case, when the activities of several neurons are recorded simultaneously, it is noted that the asynchronic form for the activity of the reticular neutrons is preserved during the initial orbit of the effect of stress. Subsequently, when the effect of accelerations with large values is continued, there is a grouping of the neuron impulses into separate volleys, between which there are periods of quiet. The quiet periods gradually become longer, and the volleys become shorter. In a number of cases, it was found that there was synchronization of several neurons. These changes in the neuron activity coincided in time with the predominance of slow oscillations in the integrated EEG. During the following periods, the described changes in the activity of the reticular neurons underwent an opposite development. Thus, the dynamics for the changes in the activity of the neurons for the reticular formation of the brain stem, and the EEG during the effect of acceleration are essentially close to the dynamics for the changes in the activity of the cortical neurons during the process of development for the phase changes in the EEG during hypoxia.

Naturally, this still-disconnected information still cannot disclose the principal physiological mechanisms causing the phase changes in the EEG. A great deal of work remains to be done in this field. From a practical point of view, the presence of phase changes in the EEG, and the rather reliable correlation of these changes with the functional changes in the central nervous system (determining the subject's working capacity), produce the possibility for using the EEG as one of the most informative parameters for constructing the systems of observation and medical control of a subject's condition during space flight, and during other extreme conditions in life. In this case, it is expedient to use the EEG in the systems of automatic observation and signaling. The first

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steps for such a development are already being devised for an automatic sensor of the hypoxic condition. In contrast with the previous designs by Prast and Noel, the program we have designed is based, not only on the indices of the EEG, but also on a calculation of the functional changes in the principal physiological systems: blood circulation and respiration. In relation to this, the depth of the hypoxic condition can be evaluated from several symptoms, i.e. on the basis of definite symptom-combinations.

Finally, we will briefly discuss the results of electroencephalographical studies, conducted during the flights on the spacecraft of "Vostok" type.

For the first space flights, with the astronauts Gagarin and Titov, the electroencephalographic studies were conducted only before and after the flight. The results of these studies did not reveal any substantial changes in the EEG after the orbital flights.

Electroencephalographic studies during flight have just begun. Therefore, the results of these first observations have mainly methodological value. However, the information collected thus far indicates that a stable telemetric recording of the EEG can be obtained during flight. However, in order to guarantee a high reliability for such a recording, we need further studies of the design of a special system for attaching the electrodes, providing for keeping them in place for many days without substantial changes in the interelectrode resistance. The EEG recordings obtained during the flights of the spacecraft "Vostok-3" and "Vostok-4" have not revealed changes in the EEG which exceed the limits of the norm. However, a full-value extraction of useful information from electroencephalographic recordings made during a space flight is possible only after a serious examination of the functional shifts in the EEG occurring in relation to the many factors which affect an astronaut's organism simultaneously and sequentially. We are speaking about the shifts in the EEG which are caused by a task carried out during the flight, the program of work and rest, daily routines, /92
emotional stress, etc. A clarification of the role of these factors, by modeling them during the process of training the astronauts, will provide in the future for comparing the electroencephalographic recordings obtained during the flight and for significantly increasing the significance of the EEG as one of the most important parameters which characterize the state of the central nervous system.

Speaking of the role of electroencephalographic studies in space medicine at the present, we must emphasize three principal aspects in which it is used.

(1) In the selection and training process, it is a very important indicator of the central nervous system's reaction to the effect of various functional tests, including those which imitate the effect of individual flight factors;

(2) It is a very important parameter in the symptom-complex, which determines the general condition of a subject during the development of severe pathological conditions (during the development of functional changes accompanied by a rapid increase of various parameters beyond the limits for the physiological norm), in relation to which it must be used for automatic sensing (aboard the craft and at the ground observation stations) of changes in the astronaut's condition;

(3) It can be used to determine the levels of wakefulness and sleep for the astronaut during various flight periods. In this case, the electroencephalographic determination of the sleep orbits is particularly valuable, since it indicates the astronaut's condition in a situation when the possibilities of actual contact with the astronaut are extremely limited.

GRAVITATIONAL FACTOR

HUMAN PHYSIOLOGICAL REACTIONS TO THE EFFECT OF ACCELERATION DURING SPACE FLIGHT[1]

P.V. Vasil'yev and A.R. Kotovskaya

ABSTRACT: The results of experimental studies, obtained during actual space flights and laboratory tests on the effect of transverse accelerations are presented in this article. A comparative analysis of the reactions for the astronauts aboard the "Vostok" and "Voskhod" is given for the effect of accelerations during a flight and during rotation in a centrifuge. The results of examining the tolerance to accelerations after a long period of hypodynamia (under conditions of strict confinement), imitating certain effects of weightlessness, are presented. Certain methods for increasing an organism's resistance to the effect of accelerations are examined (physical exercises, pharmacological methods, adaptation to hypoxia under the conditions of a pressure chamber or a high mountain).

Multiple experiments under ground conditions, in rockets, and /93
in artificial Earth satellites have presented a number of problems, of which the questions of the effect of accelerations on an organism occuring during space flight are of great importance.

The problem of the effect of accelerations includes a number of tasks, of which the principal ones are: the study of the effect of various regimes of acceleration on human working capacity and physiological functions; the examination of the mechanisms for the physiological reactions to the effect of accelerations; the investigation of physiological criteria for estimating and predicting the tolerance to accelerations; the determination of human resistance to the effect of accelerations during the period subsequent to weightlessness and other flight factors; the examination of various specific and non-specific methods and means for increasing human resistance to the effect of accelerations.

The length of time spent under conditions of weightlessness, the regimes of hygienic parameters, the particular features of working activity, and many other factors can have a substantial effect on the individual resistance of man to accelerations. There- /94

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fore, we are giving special significance at the present time to the problem of an astronaut's tolerance to accelerations which occur during landing after a long period of weightlessness, as well as to a development of certain ways and methods for increasing man's resistance to the effect of accelerations.

Results of experimental studies, obtained while carrying out actual space flights well as under laboratory conditions, and answering to some or another degree the questions presented above, are given in this article.

ASTRONAUTS' REACTIONS TO THE EFFECT OF ACCELERATIONS DURING SPACE FLIGHT

According to subjective evaluations, the accelerations occurring while craft of the "Vostok" and "Voskhod" series entered orbit were endured by all the astronauts approximately in the same way as during rotation in a centrifuge. The changes in the physiological characteristics before launching, and the reactions during the active segment of the flight, were similar for almost all the astronauts. The increase in pulse rate and respiration, occurring before launching, continued to rise at the beginning of the flight.

The pulse rate and the respiration rate reached maximum values during the first ten seconds, when the accelerations were insignificant in value. Then, despite the continuing increase of accelerations, there was a gradual reduction of the pulse and respiration rates. The changes in the time characteristics of the electrocardiogram corresponded to an increase in the rate of heart contractions. Toward the end of the active segment, the rate of heat contractions and respiration for the astronauts was usually within the limits of the values which are characteristic for the period before launching. A further decrease in the rate of heart contraction and respiration occurred much more slowly under the conditions of actual flight than after ground experiments in a centrifuge ("Vtoroy gruppovoy kosmicheskiy polet i nekotoryye itogi poletov sovetskikh kosmonavtov na korablyakh Vostok" (The Second Group Space Flight and Certain Conclusions from the Flight of Astronauts on Vostok Craft), edited by N.M. Sisakyan. Moscow, Nauka, 1965). In comparing the data from the active flight segment with the results of rotation in a centrifuge, we can see that the degree of physiological changes was much more significant under the conditions of actual flight. Moreover, in contrast to the results of laboratory studies, the data for the active sigment in actual flights in general have not provided for finding a clear dependence between the dynamics of the physiological characteristics and the values of the accelerations.

During the period when the craft entered orbit, emotional tension, in addition to the accelerations, affected the astronauts' physiological reactions. Obviously, the emotional tension greatly determined the original level and the nature of the changes in individual characteristics. The role of emotional tension becomes /95

particularly significant when we compare the values of the astronauts' physiological characteristics immediately before launching with those obtained during the action of accelerations in a centrifuge as shown in the graph for the active segment (Table 1). In almost all cases, the rate of heart contraction was much higher before launching than during anticipation of starting the centrifuge and during the action of accelerations in the centrifuge.

TABLE 1

PULSE RATE FOR CERTAIN ASTRONAUTS, 1 MIN BEFORE LAUNCHING AND DURING THE ACTION OF ACCELERATIONS IN A CENTRIFUGE

Astronauts	Pulse Rate (Maximum Value), beats/min nin	
	1 min Before Launching	During the Action of Accelerations in a Centrifuge
G. Titov	130	108
A. Nikolayev	114	82
P. Popovich	136	124
V. Bykouskiy	134	102
V. Komarov	89	80

The effect of the nervous-emotional factor, concealing the reactions to the action of accelerations, was clearly expressed in P. Belyayev and A. Leonov when the craft entered orbit. In this flight, in contrast to all the previous ones, there was a gradual increase in the rate of heart contractions toward the end of the active segment. The pulse rate continued to increase, and, after the onset of weightlessness, it greatly exceeded the level achieved during the effect of accelerations. We can assume that this shift in the cardiac activity was caused by emotional tension in relation to the imminent preparation for Leonov's "exit" from the craft into outer space.

We noted that, during the flights in the "Vostok", the changes in the physiological characteristics for the astronauts were much more pronounced than for the "Voskhod" (Table 2).

Thus, while the pulse rate for the astronauts on the "Voskhod" one minute before launching averaged 94 beats/min, for the astronauts on the "Vostok" craft it was 132 beats/min; during the active segment of the flight, it was 95 and 124 beats/min, respectively. This difference is probably determined by the lesser degree of nervous-emotional tension for the crew members in collective flights (a "feeling of fellowship"). /96

TABLE 2

PULSE RATE (AVERAGED VALUES) DURING THE ACTION OF ACCELERATIONS FOR THE ACTIVE SEGMENT, BEATS/MIN.

Astronauts	In Flight	In a Centrifuge	Difference
Yu. Gagarin	116.5	67.0	+49.5
G. Titov	113.1	77.0	+54.0
A. Nikolayev	120.6	72.3	+48.3
P. Popovich	120.8	81.5	+39.3
V. Bykovskiy	135.2	71.0	+64.2
V. Tereshkova	140	75.6	+51.7
Average	124.3	75.6	+51.7
V. Komarov	92.2	73.2	+19
K. Feoktistov	100.2	88 6	+11.6
B. Yegorov	112.7	75.5	+37.2
P. Belyayev	85.0	70.0	+15
A. Leonov	87.0	65.0	+22
Average	95.4	74.4	+21.0

The changes in the physiological characteristics of nervous and emotional origin also occurred before the landing of the craft.

Toward the end of the flight, there was an increase in the pulse rate and respiration for all the astronauts, which evidently was caused by anticipation of landing as a very serious and conclusive stage of the flight. The physiological reactions to the landing segment of the flight during deceleration of the craft in dense layers of the atmosphere, as a rule, were more pronounced than during entry into orbit. According to the statements of the majority of the astronauts, the accelerations during this flight segment were endured, subjectively, with much more difficulty than for the same in a centrifuge. For some astronauts, the pulse rate reached very high values: 168-190 beats/min. It is well known that similar changes were also recorded for the American astronauts. The amount of reaction in this case was greater than during the /97
effect of similar accelerations for rotation in a centrifuge. For most of the astronauts during the landing segment of the flight there were short-period visual disorders in the form of a blackout. Such disorders were not observed during the action of accelerations in landing simulation in a centrifuge.

The question of whether or not the above-mentioned difference in reaction to the effect of accelerations during rotation in a centrifuge in a simulated landing and during actual landing increases in relation to the length of time for the flight is of great interest.

After remaining under conditions of weightlessness for one day (Titrov, Komarov, Feoktistov, Yegorov), the difference in the pulse rate averaged +10 beats/min (with extreme values from +3 to +22 beats/min).

After 3- and 4-day flights (Popovich, Tereshkova, and Nikolavev), the difference in the rate of heart contractions increased to 30-32 beats/min, and after a 5-day flight, it reached a maximum value of 62 beats/min (V. Bykovskiy). These data encouraged us to study in greater detail the problem of human tolerance to accelerations in the landing segment following weightlessness. Actually, in carrying out the program of space research, we must know exactly what effect a long period of weightlessness can have on man. The structuring of predictions, obviously, should be based on the study of flight tests as well as on data from laboratory experiments in which the corresponding effects of weightlessness are reproduced. Immersion in water and a long period spent in a horizontal position with limited mobility are laboratory models which can be used for evaluating the effect of weightlessness on man's tolerance to accelerations.

At the present, it has been established that a long period of hypokinesia (remaining in a horizontal position) causes a decrease in an organism's resistance to physical work and orthostatic tests [9,11,17,22,26,27,28].

According to the data we have [24,17], a long period of confinement to bed resulted in significant disorders in the regulation of blood circulation, which were intensified because of weakening of the tonus of the skeletal muscles. Similar disorders in the blood-circulation system can occur in an astronaut who is returning to the Earth's gravitation after a long period of space flight.

The data on the effect of a long period of hypodynamia or immersion in a liquid on the tolerance to accelerations are of particular interest. A decline in the tolerance to accelerations, as in the case of orthostatic tests, was noted by practically all the researchers working in this area. After remaining in water for 6-24 hours [25,26,27], the subjects showed a decline in the reaction of their cardiovascular and respiration systems to an orthostatic test and the effect of accelerations, all the way to development of pre-collapse and collapse conditions.

The data on the flights of animals and man in outer space have /98 not provided for finding such serious disorders in the working capacity and the tolerance to gravitational effects as in the simulation experiments [19-22].

It is possible that the length of time the astronauts remained in orbit was insufficient for the development of processes linked with the reconstruction of activity for the cardiovascular system, imposed by the conditions of weightlessness. It is also possible

that motor activity, special physical exercises, as well as careful selection and training of astronauts for flight prevented the appearance of undesirable changes on the part of the cardiovascular system. However, we could never exclude the idea that, for longer-period flights, the debilitating effect of weightlessness on the cardiovascular system would be more pronounced if the corresponding prophylactic measures were not found. Unfortunately, studies in this direction are very limited. It seems expedient that we should set up new experiments, exposing the examinees to conditions of hypokinesia for a long period of time.

STUDIES ON THE TOLERANCE TO ACCELERATIONS IN EXPERIMENTS WITH HYPOKINESIA AND KEEPING SUBJECTS CONFINED TO A HORIZONTAL POSITION FOR A LONG PERIOD OF TIME

Twenty-one men, ranging in age from 20 to 25, participated in our experiments. Studies on the subjects' resistance to accelerations in a centrifuge were carried out by two methods: the first involved determining the maximum time for tolerance to accelerations with a value of 7 and 8 units; the second, by determining the maximum value for tolerance to an acceleration (with accelerations accumulating at a rate of 0.2 units/sec). The tolerance to accelerations was determined before hypokinesia (control rotation) and after it. The direction of the accelerations was always "chest-back". The subject was in a half-reclining position on a couch whose back was tilted at angles of 10 and 25° to the "horizontal".

The examinees were confined strictly to bed, with limited motor activity, for 8 to 15 and 20 days. In transporting them to a centrifuge after the period of hypodynamia, every caution was taken to preserve their horizontal position (transport on stretchers).

The results of laboratory studies showed that the time for maximum tolerance to accelerations of 7 units after 20-day hypokinesia in a number of cases decreased to 4-6 sec, with 4-5 min for controls. In only one case did the time for tolerance remain practically unchanged. It is interesting to note that this same examinee was in a pre-collapse condition during rotation in the centrifuge. /99

In using the second method, it was found that the maximum endurable value for an acceleration after 8-15 and 20 days of hypokinesia, decreased on the average by 2.2 units. The decrease in the subjects' resistance varied in individual cases within a range from 0.7 to 4 units.

We must note that, after hypokinesia, experimental rotations in the centrifuge were endured (subjectively) with more difficulty than were the controls, despite the smaller value of the acceleration.

It is very interesting that the achievement of equivalent values for accelerations was accompanied by greater functional break-

downs of an organism's physiological systems. Thus, for subjects exposed to an acceleration of 8-9 units, the average pulse rate was 170 ± 11 beats/min, while it was 149 ± 13 beats/min for the control rotations. We should also note that, in individual cases, the rate of heart contractions even reached 190-192 beats/min.

During the action of accelerations after hypokinesia, there was also an increase in the systolic indicator up to 70-85%, by comparison with 54-60% in the control experiments, a decrease in the voltage of the waves of the *QRS* and *T* complex and, in some cases, a decrease in the *S-T* interval. The increase for the systolic indicator was caused mainly by a significant contraction of the *R-R* interval. In individual cases, the increase for the systolic indicator during the action of overloads also occurred because of a lengthening of the electric systole which did not correspond to the given pulse rate. In one case, a negative T_1 wave was noted. In some cases, a breakdown of the rhythm of heart contractions in the form of extrasystoles of various origins was also observed during control rotations, but it was more frequent after hypokinesia.

The systolic pressure in the brachial artery, during the action of accelerations after hypokinesia, remained at lower values than in the controls. The maximum pressure in the vessels of the earlobe decreased in all cases, even despite the lower values for the acceleration to which the subjects were subjected. After stopping the centrifuge, there was in all cases a tendency for the pulse pressure to decrease because of an increase in the diastolic pressure by 15-25 mm Hg; the systolic pressure was either equal to the control values or somewhat exceeded them. For subjects who had been in a state of hypokinesia, the period for recovery of the original characteristics of the cardiovascular system after rotation increased as a rule. The recovery time was lengthened by 10-50 min. in relation to the control rotation, and lasted a total of 60 min, while in some cases it lasted 90 min.

Moreover, there were other signs of vegetative changes noted, /100 such as, for example, paleness, hyperhydrosis of the facial integument and cysts on the hands, with frequent acrocyanosis. These symptoms were also found in control rotations, but after greater accelerations.

As for the indices characterizing the function of external respiration, there were also certain changes during the action of accelerations after previous hypokinesia. The feeling of difficulty in breathing during the effect of accelerations was much stronger than during the control experiments, and in a number of cases it was one of the reasons for terminating the experiment. In this case, the acceleration of least value was the marginal one. The rate of respiration underwent very significant shifts. Thus, if in the control rotation during the action of accelerations (of 6-9 units), the rate of respiration increased by 50% (the original was taken as 100%), then after hypokinesia it increased by 114%. During

deceleration of the centrifuge and the immediate after-effects, there is usually a significant increase in respiration rate, respiration volume, and oxygen requirement, as a result of the oxygen debt occurring during the action of accelerations. After hypokinesia, the level of the oxygen debt was much higher. The increase in the respiration rate during deceleration of the centrifuge after hypokinesia reached 150% (70% in the control). The period for eliminating the oxygen debt was longer than for the control rotation.

A significant decrease in the visual acuity and the appearance of visual disorders (blurred vision and black-out) after hypokinesia occurred at lower values of acceleration than in the controls. In connection with this, the visual disorders following hypokinesia were more expressed in a number of cases than in the controls (black-out with subsequent pre-syncopic condition). For certain subjects, toward the end of confinement to bed, there were changes which indicated the appearance of increased fragility in minute vessels (the appearance of a positive endothelial syndrome), combined with changes in the size and shape of the capillaries. These phenomena were also reflected in more expressed hemorrhagic phenomena after rotation in a centrifuge.

Thus, on the basis of the studies carried out, we can conclude that even a far-from-complete simulation of the conditions of weightlessness causes a decrease in human resistance of accelerations.

Despite the lesser values for endurable accelerations after hypodynamia, there was noted a higher level of physiological shifts in the majority of the cases. The most typical feature on the part of the cardiovascular system was the intensification of tachycardia.

The shifts noted on the electrocardiograms in the form of a lengthening of the time for the electric systole which does not correspond to the pulse rate, the appearance of signs of a breakdown in excitability (extrasystole) for lesser values of the accelerations than in the control, and the appearance of a negative T_1 wave probably indicate that there is a decrease in the functional capacity of the myocardium as a result of hypokinesia. The maximum occurrence of vascular disorders (appearance of a syncopic condition, visual difficulties, a decrease in arterial pressure in the vessels of the earlobe, a decrease in the pulse pressure because of an increase in the diastolic pressure after the action of accelerations) allows us to assume that, in the decrease of resistance to accelerations after a preceding long-period condition of hypokinesia, a primary role can be assigned to the changes in the cardiovascular system. /101

A breakdown in the regulation of the vascular tonus can have great significance in this case.

Experimental data [4] show that there is a change in the rate

of incorporating control mechanisms after hypokinesia (lowering of strength, inertia, and instability in developing cardiovascular reflexes during an orthostatic and sphenostatic test, and Aschner's reflex). Changes in the tonus for the vessels of the lower extremities after a 20-day confinement to bed were noted in a rheographic examination during a passive orthostatic test [17]. Subsequently, remaining for a long period of time in a horizontal position with limited mobility caused a breakdown in the adaptivity of the cardiovascular and other systems of the organism to a change in the force of gravity. These changes were found with the aid of orthostatic tests and the action of accelerations.

Under the conditions of actual space flight, there were noted certain shifts which indicated a change in the regulation of the vegetative functions in the state of weightlessness [7,8]. It was shown that the reaction of the blood-circulation system to the effect of weightlessness has a complex character in certain orbits. The possibility that the astronauts might have vestibular-vegetative troubles during the flight, signs of fatigue, and certain shifts on the part of the cardiovascular system is not excluded [7].

All this requires development and introduction of corresponding prophylactic methods. We propose that all the possible specific and non-specific means and methods be used to increase man's resistance to the effect of accelerations after weightlessness (selection of optimal regimes for the accelerations, rational methods for selection and training, pharmacological methods, purposeful physical exercises, remaining under the conditions of high-altitude, etc.).

CERTAIN WAYS FOR INCREASING AN ORGANISM'S RESISTANCE TO THE EFFECT OF ACCELERATIONS AFTER WEIGHTLESSNESS /102

A decrease in the work of the muscles under the conditions of weightlessness, in addition to a lack of hydrostatic pressure for the blood, can be one of the possible reasons for the decrease in the functional abilities of the cardiovascular system. A weak ning of the tonus in the skeletal muscles, with a subsequent decrease in its counteraction to gravitational effects, can lead to a decline in the tolerance to accelerations, orthostatic tests, and physical stresses [11,16,17,24].

Multiple studies in the area of the physiology of sports have shown that controlled physical work is a potent method for increasing human resistance to the effect of various disadvantegeous factors in the surrounding medium: chilling, overheating, hypoxia, and other stresses [9,16]. The value of physical exercise for increasing the subjects resistance to accelerations after hyopkinesia was studied in special experiments. An analysis of the materials obtained did not show a significant difference between the reactions of the cardiovascular and respiration systems for those subjects who performed physical exercises, and for those in the control group. The time for maximum tolerance to an acceleration with a value

of 7-8 units for those subjects who performed exercises did not decrease in most of the cases (4 out of 6 cases). The lowering of the limit in value for tolerance was also somewhat less than for those subjects in the control group (without physical exercises). Most of the examinees evaluated the accelerations subjectively as being almost the same as before hypokinesia.

Thus, the imposed complex of physical exercises, although it did not bring about complete preservation of an organism's resistance to the effect of accelerations after hypokinesia, nevertheless gave an apparently positive effect.

In experiments with different types of animals, we established that there could be a substantial increase in resistance to accelerations by applying a number of pharmacological preparations [3,5, 18]. Naturally, this led us to conduct examinations for some of these methods on people.

On the basis of the pharmacodynamics of the medical preparations and the mechanism of the disorders occurring during acceleration, we found it expedient to use substances which affected various pathogenic links. In our studies, we used combinations of strychnine nitrate, caffeine, and phenamine. In this case, we obtained reassuring results which, it seems to us, open up new oaths for increasing the astronauts' resistance to the effect of accelerations after a long period spent under conditions of weightlessness.

Obviously, we can consider that properly-selected physical /103
exercises, as well as certain pharmacological preparations, will be used in practice aboard future space flights.

An attempt to stimulate general reserves of compensatory mechanisms, by using various non-specific methods, is no less important. From this point of view, it is relevant to examine the possibility of using acclimatization to hypoxia as a non-specific method for increasing man's resistance to accelerations.

It is well known that animals acclimated to the conditions of hypoxia have increased resistance to a sharp oxygen deficiency, penetrating radiation, the toxic effect of poisons, etc. At present, there is no single point of view on the mechanism of the increase in this non-specific resistance. However, it is acknowledged that stimulation of blood-circulation, respiration, and the blood system, as well as tissue factors, have considerable significance [1,23].

At present, thanks to the large number of studies, it has been established that during the action of long-period transverse accelerations, one of the principal pathogenetic mechanisms is the development of an oxygen deficiency which has a circulatory and hypoxic nature [2,6,12-14]. Therefore, we find it expedient to determine the possibility for using acclimatization to high-moun-

tainous conditions as a method of non-specific training for man, in order to increase his adaptive possibilities and, subsequently, his resistance to a number of extremal flight factors (accelerations in particular).

The studies were conducted on animals (white mice, rats, guinea pigs, rabbits), and young, healthy people also participated. Highly-qualified mountain climbers, who had been under high-mountain conditions 1-2 months out of every year for more than 10 years, and also people who had not been trained for high altitudes, participated in the experiments.

Adaptation to hypoxia was carried out at the high-mountain camp at Terskol, and in pressure chambers. Various schemes of non-continuous (in a pressure chamber) and continuous adaptation on a high mountain were evaluated. The person's individual resistance to the effect of accelerations in a centrifuge was determined in two control rotations with maximum-endurable value. The "chest-back" acceleration was produced while their couch was tilted at an angle of 25° to the "horizontal".

In experiments with animals, it was established that the survival rate for acclimated white mice, rats, and guinea pigs during the action of large accelerations was 1.5 - 2 times higher than for the control animals. This effect was preserved for the first two or three weeks after termination of acclimatization.

Breakdowns in the function of the cardiac activity, according to data from electrocardiograms, occurred later for the experimental animals, and they were less pronounced. /104

The animals' active adaptation to high-mountain conditions during systematic physical training was more effective than a passive stay at a high altitude. In the first case, the survival rate during the effect of accelerations was 25% higher than in the second.

In the studies where people participated, it was established that the mountain-climbers, despite a long interval after the last time they were in the mountains (10-11 months), were more resistant to accelerations than untrained people. Thus, while the limit for tolerance to an acceleration for the non-trained subjects averaged 9.5 units, it was 11.0 units for the mountain-climbers.

After staying at the high-mountain camp, the most positive effect from the point of view of tolerance to accelerations was observed during the first few days (3 days). The resistance to accelerations increased by $\pm$ 2.4 $\pm$ 0.2 units for the untrained people, and somewhat less for the mountain-climbers (by +1.5 $\pm$ 0.2 units). The level of resistance to accelerations decreased by 0.6 - 0.8 units after a month, but it still exceeded the original data by +1.3 - 2.0 units.

During rotation in a centrifuge after staying under the high-mountain conditions, the increase in the pulse rate was 4 - 30 beats/min, and respiration decreased by 5-10 cycles/min, in comparison with the control experiments. In a number of cases, the effect of accelerations after staying in a high-mountain locality was not accompanied by breakdowns in the rhythm of the cardiac activity, which had been recorded for the same subject during the control rotation.

Therefore, at the present time, there have been found certain methods for non-specific training and directed actions on human functional systems, which can be used for further development in the process of preparing astronauts for increasing their resistance to various flight factors, including accelerations.

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HUMAN PHYSIOLOGICAL REACTIONS DURING THE ACTION OF TRANSVERSE ACCELERATIONS FOLLOWING HYPODYNAMIA

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ABSTRACT: The physiological reactions to, and tolerance for accelerations were studied in tests on subjects following hypodynamia which lasted from 7 to 20 days. Examinations were made of the bioelectric activity of the heart, the cerebral cortex, the function of external respiration, the arterial pressure, and the visual function. The decrease in tolerance to accelerations in all cases averaged 2 units, and did not depend on the duration of hypodynamia. Physiological reactions to accelerations were greater following hypodynamia. The decrease in tolerance to accelerations was caused mainly by a disorder in the regulation of the vascular tonus.

The problem of human resistance to the effect of accelerations /106 following weightlessness is now one of the central problems in space medicine. In fact, when carrying out programs for space research, we must know what effect a long period of weightlessness can have on a man, during space flight and after return to the Earth.

The proposed methods for physiological simulation of certain, very important effects of weightlessness (such as immersion in water, lengthy confinement to bed) provide only preliminary answers to certain questions regarding this problem. In many studies by foreign and Soviet authors, it has been shown that there is a decrease in the functional abilities of various physiological systems of an organism following hypodynamia under laboratory conditions. In particular, many authors [2,5,6,10,12,13,15,19,20] have observed a decrease in resistance to physical stress and to an orthostatic test following hypodynamia lasting 6 hours to 4 weeks. Certain researchers attribute great significance to a decrease in the volume of the blood plasma and to the quantity of electorlytes under these conditions [14,16,17,19,21].

The flights of Soviet and American astronauts have shown that a similar decrease in the functional abilities of the human organism also occurs under the conditions of actual flight. In particular, in the case of American astronauts in a state of weightlessness for up to 8 days, there was a decrease in orthostatic stability after the flight. The average length of the recovery period of orthostatic tolerance was 47 hours and the maximum was 104 hours. Moreover, the astronauts Cooper and Conrad, during their 8-day flight,

showed an increase in the amount of erythrocytes, with a decrease in the plasma volume, a decrease in the calcium in the bones, and the appearance of edema in the leg region [11]. The phenomena of decalcination and edema of the legs was also observed in the previous flights of Cooper and Schirra [22].

After the flights of Soviet astronauts on craft of "Vostok" and "Voskhod" type, functional cardiovascular tests (passive orthostatic test, test with measured stress) in a number of cases revealed certain features of the physiological reactions. Thus, for example, in the case of the astronauts P. Popovich, V. Tereshkova, and V. Bykovskiy, the increase in the pulse rate for physical stress after /107
the flight was somewhat greater, and the period of recovery to the original level lasted longer, than before the flight [3, 8]. For K. Feotistov and B. Yegorov, it was noted during the stress that there was a decrease in the beat and minute volumes by 26-47%, and a decrease in the pulse pressure by 10-24 mm Hg [4].

We have reason to assume that the most probable cause for the appearance of the above-described changes is the factor of tolerance. Naturally, in this case we cannot disregard the etiological role of emotional stress, the effect of position, and other factors of space flight. However, the conformity of the physiological signs characterizing the state of a human under the conditions of hypodynamia and weightlessness favor the assumption which we have given.

We are of the opinion that, in view of man's future conquest of outer space, substantial significance should be given to the direct effect of the weightlessness factor. In this case, not only the effects related to man's transition to normal gravitation on the Earth, but also his tolerance to accelerations (which can reach high values during landing) are of particular significance.

Data on human tolerance to acceleration following weightlessness were obtained for orbital flights which lasted from one to five days [1]. In particular, an analysis of the increase in the rate of heart contractions during the effect of acceleration for the landing segment of the flight showed the following: Following a state of weightlessness for one day, the increase in the pulse rate for 4 astronauts, in comparison with the data from a centrifuge, averages +10 beats/min, with extreme values from +3 to +22 beats/min. After flights which lasted 3-4 days, the increase in the rate of heart contractions for 3 astronauts was 30-32 beats/min, and after a 5-day flight, it achieved a maximum value of 62 beats/min.

These data show a definite decrease in human tolerance to accelerations, shown by the increase in pulse rate relative to centrifuge conditions.

However, at the present time we cannot answer questions related to the change in resistance to accelerations for longer periods of

time during space flights. In this regard, certain authors have recently begun to conduct studies examining the effect of a long period of hypokinesis on human tolerance to transverse accelerations.

Miller and Leverett [18] studied the effect of transverse accelerations, with a landing profile for the "Gemini" craft (peak of 10.6 units) in 22 subjects, after they were confined to bed for four weeks. In this case, the authors did not succeed in finding a reliable difference in the level of individual tolerance, indicated by disorders in the central vision. At the same time, the pulse /108 rate at the peak acceleration increased on the average by +35 ± 20 beats/min, in comparison with control rotations.

In our previous studies [7], we showed the change in tolerance to transverse accelerations after 20 days of confinement to bed. The maximum time for tolerance to accelerations of 7 units after hypokinesia in certain cases decreased to 4-6 sec, with 4-5 min for the control rotation. Moreover, we noted great changes on the part of the indices for the cardiovascular and respiration systems during rotation following hypokinesia (in comparison with controls), slower recovery during the subsequent period, a more pronounced decrease in visual acuity, and a worsening of feeling.

The purpose of these studies was to examine the effect of a long period of hypodynamia on human resistance to transversely-directed accelerations. In order to determine the tolerance, we used the effect of a peak acceleration with a constant rate of increase (0.2 units/sec) until the appearance of the first signs of functional disorders on the part of an organism's physiological systems. The back of the seat was tilted from a "horizontal" position to angles of 10° and 25°.

For an objective analysis of the examinee's condition during accelerations, and also before and after termination of the acceleration, we made recordings of the electrocardiogram in 3 intervals according to Nebbe, as well as the rate of respiration, the maximum arterial pressure in the brachial vessels and the earlobe, the electroencephalogram, and the latent period for simple sensory and motor reactions to light; we determined the visual acuity, and in some cases the respiration volume. The electroencephalogram was recorded in two fronto-parietal and 2 unipolar intervals (frontal and parietal to the left). The rest of this study method did not differ from the one described previously [7].

The principal criterion for calculating human tolerance to acceleration was the change in the maximum endurable value for acceleration, the changes in the indices of the principal physiological functions, and the length of time for their recovery during the subsequent period.

Ten subjects participated in the studies. They underwent preliminary clinical observations. The length of time for hypodynamia

(strict confinement to bed) varied from 7 to 20 days (Table 1). The subjects were divided into two groups: for 6 subjects, the tolerance to accelerations was determined for a seat-back tilted at an angle of 10°; for 4 subjects, the seat was tilted at an angle of 25°. The tolerance to acceleration was determined before hypokinesis (control) rotations) and after it. The average value for the maximum endurable acceleration was higher for those in the first group than for those in the second (error less than 1%). This relationship was also obtained after hypodynamia. However, the average values for the decrease in tolerance to accelerations following hypodynamia among those in the second group did not show statistical reliable differences (Table 1). /109

TABLE 1

CHANGE IN TOLERANCE TO ACCELERATION FOLLOWING HYPODYNAMIA

Subj.	Length of Hypodynamia days	Angle of Tilt For Seat-Back in a Centrifuge (in °)	Maxim Endurable Acceleration, units			Criterion For Tolerance	
			Before Hypodynamia	After Hypodynamia	Difference	Before Hypodynamia	After Hypodynamia
Sh-k	7	10	12.0	9.8	-2.2	Blurred Vision	Black-out
B-k	7	10	14.0	12.9	-1.1	Diff. in Breathing	Diff. in Breathing
Kh-vI	10	10	14.0	12.0	-2.0	Blurred Vision	Blurred Vision
L-y	15	10	15.0	11.0	-4.0	Diff. in Breathing & Blurred Vision	Blurred Vision
B-y	15	10	14.0	11.8	-2.2	Extrasystole	Blurred Vision
G-a	20	10	13.8	12.3	-1.5	Diff. in Breathing	Blurred Vision
G-n	8	25	9.5	7.8	-1.7	Blurred Vision	Blurred Vision
G-v	9	25	11.0	9.0	-2.0	Blurred Vision	Diff. in Breathing
Kh-vII	12	25	10.2	9.0	-1.2	Blurred Vision	Black-out for 9 units, syncope
T-n	12	25	9.0	6.8	-2.2	Blurred Vision	Black-out
Aver. Data	7–20	10	13,8±0,9	11,6±1,0	−2,2±1,0 $n=6$		
	8–12	25	9,9±0,9	8,1±1,0	−1,8±0,4 $n=4$		

Note: n is the Number of Cases.

In making a comparison with the duration of hypodynamia, we did not succeed in find a reliable correlation (R = 0.2) between the duration of hypodynamia and the degree of increase in tolerance to accelerations. As we can see from Table 1, for the subject Sh-k, who was subjected to hypodynamia for the shortest length of time, the decrease in tolerance (-2.2 units) was greater than for the subject G-a, who endured hypodynamia for 20 days (-1.5 units).

The decrease in resistance to accelerations was correlated with subjective sensations. Thus, after hypokinesia, experimental rotations in seven out of the ten cases were endured with more difficulty (subjectively) than in the controls, despite the lesser value for the acceleration achieved. /110

For the effect of an acceleration, before hypokinesia, characteristic changes in the electrocardiogram were observed in all cases: a general decrease in the voltage of the waves and an increase in the systolic indicator to 54-58% because of a relative lengthening of the electric systole; in a number of cases, there were disorders in the rhythm, in the form of extrasystole and relative bradycardia (Table 2).

In the initial state, changes were noted in the electrocardiogram after hypokinesia: a decrease in the voltage of the waves by a factor of two or more, an increase in the systolic indicator by 11-23% in comparison with the control (obviously linked with considerable narrowing of the *R-R* interval), in some cases a compression or electronegativity of the *T* wave (greater in the first interval). These changes are obviously related to the effects of hypodynamia. We also cannot disregard the additional effect of emotional excitation on the value of the *R-R* interval and the systolic indicator during rotation.

In analyzing the characteristics of the physiological reactions caused by the effect of an acceleration following hypokinesia, the most typical feature was an increase in the recovery period and a change in several characteristics (pulse rate, external respiration, electroencephalogram, etc.). In all the cases, the pulse rate during the effect of an acceleration with one and the same value was higher after hypodynamia than in the control. Thus, for an acceleration of 8-9 units, the average pulse rate after hypokinesia was 168 $\pm$ 12, with 150 $\pm$ 12 beats/min for the control rotation.

After hypokinesia, the value for the compression of the *T* wave during rotation remained practically constant in comparison to the control rotation. In one case (Kh-v II), there was intensification of the electronegativity of the T_{II} wave. The systolic indicator increased in all cases up to 70-83%. This increase was caused mainly by a more significant contraction of the *R-R* interval. In only one case, after hypokinesia for 15 days, there was also an increase in the systolic indicator during acceleration because of a lengthening of the electric systole, not corresponding to the given pulse rate for 0.07-0.09 sec (instead of 0.03 - 0.06 sec in the control).

The systolic arterial pressure in the brachial vessels (measured during action of an acceleration in 2 subjects in 3 experiments) remained at lower values after hypokinesia than in the controls. The maximum pressure in the vessels of the earlobe during the control rotation increased in 2 out of 3 cases, while it decreased in all cases after hypokinesia, despite the lower values for the maximum

TABLE 2: CHANGE IN CERTAIN CHARACTERISTICS OF THE CARDIOVASCULAR SYSTEM DURING ACCELERATION (BEFORE AND AFTER HYPODYNAMIA)

Examinee	Pulse Rate, beats/min						Arterial Pres., mm Hg			Features of the EKG	
	During accel., 8-9 un.			Recording Dur., min.			Diff. Bef. and After Accelerations			Before	After
	Bef.	Aft.	Diff	Bef.	Aft.	Diff	Bef.	Aft	Diff.		
Kh-vI	150	175	+25	20	55	+35	+35/ +20	-	-	In Descent, Relative Bradycardia; Single εx's at 30 beats/min	One εx During Descent
L-y	132	152	+20	5	50	+45	+30/-5	+20/+20	-10/+25	None	None
B-y	160	174	+14	20	52	+32	+20/0	+50/+30	+30/+30	Single εx's for Max. Accleration	Single εx's for Maximum Accel.
G-a	138	150	+12	10	60	+50	+25/0	+15/-15	-10/-15	None	None
G-n	150	160	+10	5	20	+15	+5/-	+35/-	+30/-	None	None
G-v	160	180	+20	5	5	0	0/-	+10/-	+10/-	None	One εx for 8 units
Kh-vII	162	180	+18	29	80	+51	+25/+10	+65/+5	+40/-5	None	Intensification of the Negative T_I w/ Increas. Accel.
T-n	108	108	0	5	20	+15	-5/0	+20/+10	+25/+10	None	Negative T_I with 3 units.

Note: εx is the Extrasystole of Gastric Type.

acceleration achieved. The systolic and diastolic pressure in the brachial vessels was determined in 7 subjects following the effect /112 of accelerations. In three cases, the diastolic pressure tended to increase by 10-35 mm Hg. In five cases, there was an even greater increase in the systolic pressure. In only one case did the systolic and diastolic pressures remain at lower values (-10 -15 mm Hg). The recovery period for the cardiovascular characteristics increased following hypokinesia in all cases by 15-51 min, in comparison with the control rotation.

The latent period for simple sensory reaction to light during the effect of acceleration following hypokinesia did not differ substantially from the control.

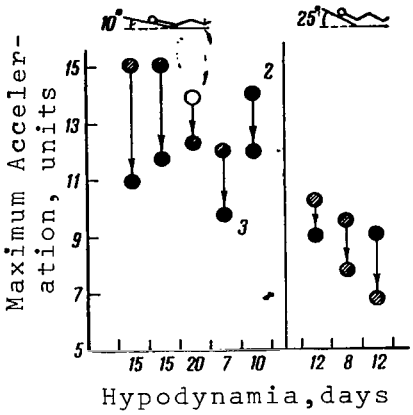

Fig. 1. Visual Troubles in Subjects during Effect of Accelerations Following Hypodynamia of Varying Length. The Upper Circles Denote the Control Data; the Lower Ones Denote the Data Obtained After Hypodynamia. (1) No Visual Troubles; (2) Blurred Vision; (3) Black-out.

A significant decrease in the visual acuity, and the appearance of visual troubles (in the form of blurred vision and black-out), in all cases following hypokinesia, occurred for values of the accelerations which were 2.5 $\pm$ 1.1 units less than in the control rotation. In this case, the level of visual troubles in 4 out of 8 cases was intensified at the peak acceleration (Fig. 1).

As for the external respiration, the following changes were observed during the effect of accelerations: According to the subjective data, breathing became intensified and difficult during the action of acceleration. In certain cases, this was one of the reasons for terminating the experiment.

The general picture for the change in the average rate of respiration before and after hypokinesia is shown in Figure 2. If, in the control rotation during the effect of accelerations from 6 to 9 units, the rate of respiration increased by 50% in comparison to the original (taken as 100%), then after hypokinesia this increase was equal to 114%. The greatest increase in the rate of respiration occurred after terminating the action of an acceleration which had maximum value. In this case, the rate of increase was much higher; at a level from 11 to 7 units, it was 70% in the control rotation and 150% after hypokinesia. The pulmonary ventilation and respiration volume were measured for 3 subjects (Kh-v I, B-y, and L-y).

The particular feature of the dynamics for the changes in these characteristics was that the curves, in all the cases, had a two-hump character (Fig. 3). At the beginning of the action of an acceleration in the control rotation, there was an increase in the pulmonary ventilation because of an increase in the respiration volume as well as the rate of respiration. In achieving a maximum value for the acceleration, there was a decrease in the value for pulmonary ventilation, with a rather high respiration rate. The second maximum increase in the characteristics of the external respiration was observed during descent, and exceeded the initial ascent in value. In this case, intensification of the pulmonary ventilation also occurred primarily because of the respiration volume. Following hypokinesia, the character of these changes for the external respiration did not change during the effect of an acceleration. At the beginning of the action of an acceleration, there was an increase pulmonary ventilation by 3.3 times, and in the respiration volume by 2.2 times, in comparison with the control. However, the level of the curves increased significantly. Similar relationships were also observed during deceleration of the centrifuge. /113 /114

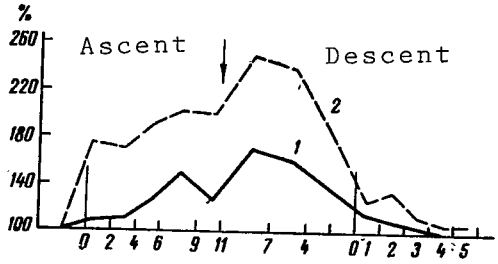

Fig. 2. Change in the Rate of Respiration for Subjects during the Action of Accelerations Before (1) and After (2) Hypodynamia (Averaged Values for 6 Subjects).

The time required for recovery of the characteristics for external respiration was more than 6 min after hypokinesia; it was 2-3 min in the control rotation.

In comparing the data for the electroencephalogram in its

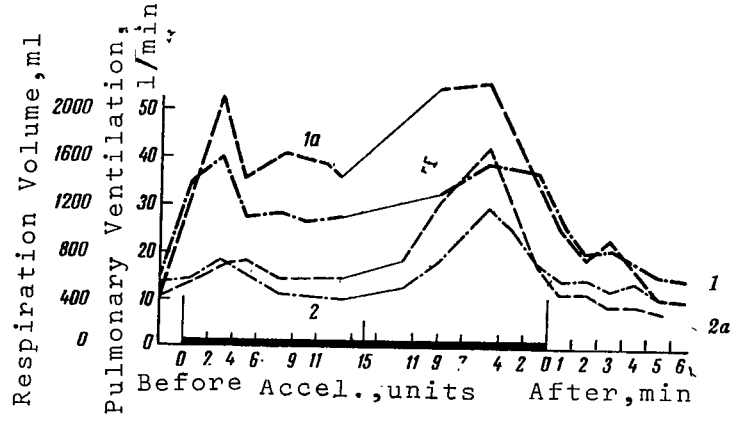

Fig. 3. Dynamics for the Changes in the Characteristics of External Respiration for Subject B-y during Accelerations During and After Hypodynamia. (1) Pulmonary Ventilation; (2) Respiration Volume: Before Hypodynamia (1a) and (2a): The Same, After Hypodynamia.

original state with the data for before and after hypodynamia, characteristic changes were found. In all 7 cases, there was an increase in the amplitude of the α-rhythm, sometimes by 2 to 2.5 times. In 5 cases (G-n, G-v, B-y, L-y, and Kh-v II), we found a shift in the α-rhythm rate toward the left, with the appearance of slower rhythms; in the other two cases, we found an increase in the rate and the appearance of irregularity in the α-rhythm. In 3 cases there was lengthening of the latent period for exaltation of the α-rhythm, when the subjects' eyes were closed from 0.2 - 0.5 to 0.7 - 0.8 sec. These changes should probably be related to the effect of hypokinesia, since the character of the electroencephalogram recovered completely after the action of an acceleration. However, in one case (Kh-v I), the shift in the rate of the α-rhythm (from 10 to 13 sec) in the initial state following hypokinesia did not tend to recover even during the period following the acceleration. In this case we cannot deny the additional effect of emotional excitation.

This condition can be substantiated indirectly by the data obtained by studying the cardiovascular system. The increase in the pulse rate before the beginning of rotation, linked mainly with the emotional factor, was significantly high in 5 out of 8 cases after hypokinesia (Table 3).

During the period following the accelerations, these changes had a tendency to "recover", i.e. there was a more significant synchronization of the rhythms, with the appearance in a number of cases of θ- and Δ-waves for open or closed eyes, and a shortening of the latent period for "exaltation" of the α- rhythm.

In 5 subjects whose electrocardiograms were recorded with unipolar leads, we succeeded in finding a greater expressivity for these phenomena of synchronization at the frontal lead. Following hypokinesia in 3 out of 4 cases, in comparison with controls, the recovery period for the characteristics of the electroencephalogram was lengthened by 4-19 min. This lengthening of the period for normalization of the electrocardiogram was most significant for those with the greatest decrease in resistance to accelerations. For the subject Kh-v I, whose resistance to accelerations changed insignificantly (-1.2 units), the length of the recovery period after hypokinesia was equal to the original. Thus, in all cases, we found a decrease in the bioelectric activity of the cerebral cortex for an acceleration on the synchronization of rhythms, with a lengthening of the recovery period for the characteristics of the electroencephalogram after hypokinesia.

TABLE 3

CHANGE IN SOME CHARACTERISTICS OF THE ELECTROENCEPHALOGRAM AND THE RATE OF HEART CONTRACTIONS, AFTER HYPODYNAMIA. /115

Subj.	Change in the Max. Tol. Units	Inc. in the Pulse 1 min. bef. Begin. of Rotation in a Centrifuge			Val. for the Latent Per. (in sec.) for "Exaltation" of α-Rhythms at 5 min. before Rotation			Length of Time for Rec. of the Char. of the EEG After Acceleration, Min.		
		Bef.	Aft.	Diff.	Bef.	Aft.	Diff.	Bef.	Aft.	Diff
Sh-k	-2,2	+9	+3	-6	0,3	0,5	+0,2	3	7	+4
B-k	-1,1	0	+6	+6	0,5	0,7	+0,2	5	10	+5
Kh-vI	-2,0	+12	+48	+36	0,5	0,8	+0,3	3	16	+13
L-y	-4,0	+6	+18	+12	0,3	0,7	+0,4	7	26	+19
B-y	-2,2	+18	+36	+18	0,2	0,7	+0,5	3	7	+4
G-v	-2,0	+18	+12	-6	-	-	-	5	7	+2
Kh-vII	-1,2	+6	+18	+12	0,3	0,6	+0,3	16	>12	<-4
T-n	-2,2	+6	-6	-12	0,4	0,9	+0,5	3	7	+4
Average Difference				+7±15			+0,34±0,13			+7,3±6
Reliability of the Diff.				<0,95			>0,999			>0,99

Note: In the Last Column, the Subject Kh-vII was Excluded from Statistical Analysis.

An analysis of the physiological reactions showed that despite the lesser values for the accelerations achieved after hypodynamia, there was a higher level of physiological shift in most cases. The most typical features involving the cardiovascular system was the intensification of tachycardia, the decrease in the systolic pressure in the vessels of the ear, the increase in the recovery period for the physiological characteristics, and sometimes a relative increase in the length of the electric systole which did not correspond to the pulse rate. Moreover, a lower threshold was found for the appearance of visual disorders after hypokinesia, by comparison with controls.

An essential feature of the reaction of the cardiovascular system to an acceleration was found in the lack of bradycardia after hypokinesia, which occurred in half of the cases for control rotations, at high values for the maximum acceleration achieved. However, in some cases following hypokinesia single extrasystoles with lesser values were found for the acceleration than in the controls; a negative T_I wave and an intensification of its electronegativity /116 during acceleration were also observed. These changes probably show that there is a decrease in the functional capacity of the myocardium as a result of hypodynamia. There is a greater number of

vascular disorders: the appearance of a syncopic condition in one case, more pronounced visual difficulties, a decrease in the auricular arterial pressure during the action of an acceleration, an increase in the diastolic pressure after its termination. These data show the significance of disorders in regulation of vascular tonus during a decrease in resistance to accelerations after hypokinesia.

The nature of the changes in external respiration show that while the acceleration is acting, there is an oxygen deficiency which is eliminated after its termination.

Considering the more significant intensification of the pulmonary ventilation after hypodynamia, during the deceleration stage in the centrifuge, we should assume that the degree of oxygen debt was greater than in the control.

The changes in the electroencephalogram in its original state after hypokinesia coincide with the data obtained by R.P. Stelkova [9] for hypodynamia lasting 7 days. The decrease in the level of bioelectric activity and the intensification of the slow rhythmicity, caused by the effect of an acceleration, indicate that there is a decrease in the excitability of the cerebral cortex after hypokinesia. In some cases, the picture of the bioelectric activity is complicated by the intensification of emotional excitation before the action of an acceleration. After rotation, there was an intensification of these changes with an increase in the recovery period (in comparison with the control). The mechanisms of the changes in the bioelectric reaction of the cerebral cortex under these conditions require further study.

The data obtained from our studies show that hypokinesia which lasts from 8 to 15 days leads to a decrease in the resistance to accelerations (-2.0 ± 0.7 units on the average). The rate of decrease in tolerance varied in our studies for different subjects (from -1.2 to -4 units), and did not depend reliably on the length of time for hypokinesia.

The data obtained on the decrease in tolerance indicate that in carrying out long space flights it will be necessary to use a number of measures for increasing the resistance of the human organism to accelerations when the craft is landing.

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THE MECHANISM OF THE CHANGE IN CARDIAC ACTIVITY DURING TRANSVERSELY-DIRECTED ACCELERATIONS

V.Ye. Belay, P.V. Vasil'yev, G.D. Glod, and V.G. Petrukhin

ABSTRACT: The effect of long periods of transversely-directed accelerations is accompanied by intensive expenditure of glycogen in the myocardium and liver. The degree of the disorders in cardiac activity during accelerations is correlated with the amount of glycogen in the myocardium. One of the pathogenic links in the exhaustion of the compensatory mechanisms for cardiac activity during long periods of transversely-directed accelerations is probably the rapid decrease in the mocardial energy resources. The normalization of elements in the electrocardiogram during the period of after-effects from acceleration is not an indicator of complete recovery of myocardial function.

In this article, we are attempting to study certain mechanisms /118 for the breakdown in cardiac activity during action of accelerations. The data we have in the literature [10, 12] indicate that one of the causes for the exhaustion of an organism's adaptation resources can be overexertion of the heart as a result of a breakdown in the metabolic processes in the myocardium and, in particular, a sharp decrease in the amount of glycogen. In relation to this, we found it expedient to clarify immediately the relationship between disorders in cardiac activity and changes in the amount of glycogen in the myocardium.

The studies were conducted on 19 mongrel dogs of both sexes, which weighed 8-12 kg (6 of these animals were controls). Accelerations with values of 12 units were reproduced in a centrifuge with an arm length of 4.2 m. The vector of the acceleration was directed perpendicular to the lengthwise axis of the body ("chest-back"). The rate of acceleration and decceleration was 0.4 units/sec. The nature of the heart's reaction to the effect of the accelerations was evaluated according to the changes in the electrocardiograms during standard intervals before, during, and after rotation. 22-30 min after rotation, the animals were sacrificed and subjected to pathomorphological examinations. The amount of glycogen was determined for small fragments of the heart and the liver by the histochemical method according to A.G. Shabadash. Together with the physiological and morphological examinations in the experiments, the functional state of the vegetative nervous system for 20 rabbits and 23 dogs was studied before and after accelerations, according to their reaction to

mediators (adrenalin, acetylcholine).

The effect of the accelerations caused regular changes in the dogs' cardiac activity [4, 5, 7, 9]. In this case, there was tachycardia and arrhythmia, expressed in various degrees, in 8 of the animals; for 5 dogs, the tachycardia shifted to a gradually or rapidly occurring decrease in the rate of heart contractions. On the electrocardiograms, there were extrasystoles; the *ST* interval shifted relative to the isoline, and the *T* wave increased sharply. The appearance of these signs showed that there was a collapse of the compensatory and adjusting mechanisms for cardiac activity, and this was a signal to terminate the effect. After 1-5 minutes, the rate of heart contractions and the elements of the electrocardiogram returned to their original level.

The results of the experiments are given in Table 1. From the data presented, we can see that the margin for tolerance to accelerations of a given value was not identical for various dogs. Thus, for 3 out of 4 animals, the signs of collapse in compensation occurred after a 3- to 7- minute application, for 1 dog after a 14-minute application, and for 1 only after 60 min. At the same time, 2 dogs were subjected to rotation in the centrifuge which showed no signs of exhaustion of the adjusting mechanisms.

For 5 animals, for whom there were definite disorders in cardiac activity, the glycogen content in the myocardium decreased sharply. For three animals, glycogen was found only in the form of very small grains in individual fibers beneath the endocardium (Fig. 1), while it appeared in groups of fibers for two animals. Even in the sarcoplasm of the muscular fibers for the conducting system (Purkinje fibers), which are usually very rich in glycogen, the

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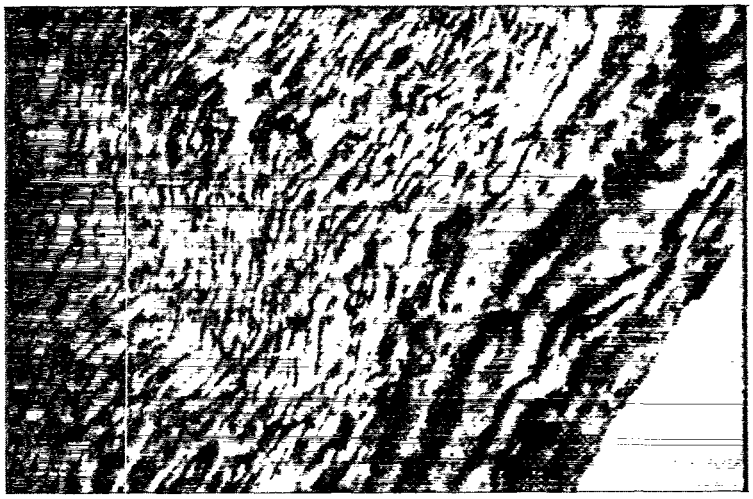

Fig. 1. Decrease in the Glycogen Content in the Purkinje Fibers of the Left Ventricle of the Dog Heart (Shabadash, 32 x 6).

TABLE 1. CHANGES IN THE CARDIAC ACTIVITY AND THE AMOUNT OF GLYCOGEN IN THE MYOCARDIUM AND THE LIVER OF DOGS, DURING THE EFFECT OF LONG PERIODS OF TRANSVERSELY-DIRECTED ACCELERATIONS /119

Experiment number	Time of Action, min	Reaction	Time for Sacr. dogs after Action, Min.	Amount of Glycogen	
				Myo-Card.	Liver
1	3	Bradycardia, Extrasystole, Shift of *ST*, Increase in *T*. "Collapse in Compensation"	25	++	+
2	60	Arrhythmia, Bradycardia, Single Ventricular Extrasystoles, Sharp Shift of *ST*. "Collapse in Compensation"	24	+	++
3	14	Arrhythmia, Bradycardia, Shift in *ST*. "Collapse in Compensation"	26	++	++
4	3	Arrhythmia, Bradycardia, Grouped Vent. Extrasystole Shift in *ST*. "Collapse in Compensation"	22	+	-
5	7	Arrhythmia, Bradycardia, Grouped Vent. Extrasystoles "Collapse in Compensation"	30	+	+
6	3	Arrhythmia, Tachycardia, Appearance of Bradycardia	22	+++	++++
7	3	Tachycardia, Insignificant Changes in the *ST* Interval and the *T* Wave.	28	+++	++++
8	3	Tachycardia, Insignificant Changes in the *ST* Interval	26	+++	++++
9	7	Tachycardia	25	+++	+
10	9	Same	23	+	+++
11	40	" "	25	+++	+++
12	4	" "	23	+++	++
13	40	" "	23	+++	+
14 - 19 (Control)	-	- -	-	++++	++++

Note: Glycogen in the Myocardium: + = Tiny Grains in Single Fibers Under the Epicardium, Decrease in Purkinje Fibers; ++ = Micro-Granular Lumps in Groups of Fibers; (Continue next page)

Note Table 1 cont.: +++ = Appearance of Large Lumped Elements; ++++ = Normal Amount.

Glycogen in the Liver: + = Micro-Granular Elements in Single Cells; ++ = Micro-Granular Elements in Groups of Cells; +++ = Appearance of Macro-Granular Elements; ++++ = Normal Amount.

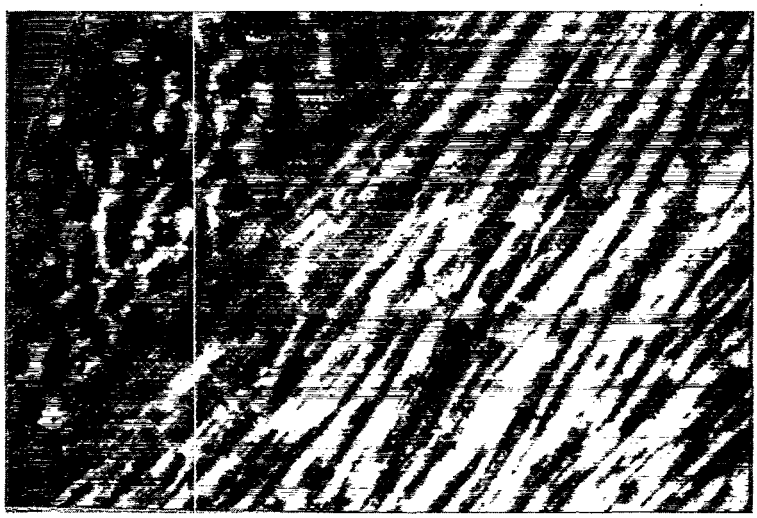

Fig. 2. Normal Amount of Glycogen in the Purkinje Fibers of the Left Ventricle of the Dog Heart (Shabadash, 32 x 6).

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Fig. 3. Decrease in the Amount of Glycogen in a Dog Liver (Shabadash, 32 x 6).

percentage decreased significantly, and the large-scale lumped elements disappeared almost completely.

For the animals who did not show signs of collapse in compensation of cardiac activity, the glycogen content in the myocardium remained at a higher level in 7 out of 8 cases during the action of accelerations. In the cores of the conducting system, its percentage did not decrease. In the groups of regular fibers, together with small-size lumps of glycogen, large lumps of glycogen (Fig. 2) were also found. In the case of one dog, the histochemical picture of glycogen in the myocardium was the same as for those animals which showed clear signs of a collapse in compensation of cardiac activity. Approximately the same differences were also observed in studying the glycogen content in the liver. Thus, a sharp decrease in glycogen content was noted for all 5 dogs who had definite disorders in cardiac activity. In this case, we found micro-granular glycogen only in single cells or in groups of them, primarily around the collecting veins (Fig. 3). /122

Nevertheless, for the majority of the animals who showed no signs of a collapse in the compensation of the cardiac activity, the percentage of glycogen in the myocardium and liver was higher during the action of accelerations (Table 1).

Thus, during the action of transversely-directed accelerations, there is a definite relationship between the degree of disorder in the cardiac activity and the glycogen content in the myocardium and liver.

The metabolism in the myocardium is characterized by a predominance of aerobic processes (consumption of glucose, fructose, and lactic acid in the blood). Moreover, the small quantity of glycogen (about 0.5%) which is expended by the myocardium only in exceptional cases serves as an additional reserve for the myocardial energy exchange [13].

It is well known that transversely-directed accelerations can be accompanied, under certain conditions, by significant disorders in humodynamics and thus by increased stress on the myocardium [4-6]. There can also be hypoxia for the myocardium as a result of a breakdown in the oxygenation of the blood in the lungs [1, 5, 6, 15, 16]. The combination of an increased stress on the myocardium and its hypoxia leads to expenditure of the "natural" glycogen, since in this case the use of lactic acid is made much more difficult [8, 10, 14]. Subsequently, one of the pathogenic links for the collapse in the compensatory-adjusting mechanisms of the cardiac activity during accelerations is obviously the overstrain in intensity for the myocardial exchange processes under the conditions of oxygen deficiency, which calls for the use of natural energy resources.

It is well known that a decrease in glycogen content in the myocardium is also observed during significant physical stress [10].

However, the mechanism of these changes apparently differs substantially from disorders occurring during the action of accelerations. The clear parallel between the disorders in the electrocardiogram elements and the change in the glycogen content in the myocardium during physical stress serves as proof of this statement. At the same time, during the period of after-effects from transversely-directed accelerations, the electrocardiogram does not completely reflect the state of the energy resources and the functional capacities of the myocardium.

We also have not excluded the idea that breakdown in carbohydrate metabolism is one of the causes for the change in the cardiac reaction (during the period following acceleration) to glucosides (strophanthin). It has been established that the sensitivity of the heart to strophanthin increases sharply under these conditions. In this regard, the degree of change in reactivity is directly dependent on the degree of the disorders in cardiac activity during the action of accelerations [2]. A similar rule was also established in relation to the glycogen content in the myocardium. /123

It is reasonable to assume that the breakdown in the carbohydrate metabolism in the myocardium is not the only cause for the exhaustion of the adaptational mechanisms of cardiac activity. Important significance probably also should be assigned to the breakdown of the functional interrelationships between the sympathetic and parasympathetic centers for the regulation of cardiac activity and the correcting effect of the higher divisions of the central nervous system, which occurs during the action of accelerations.

In particular, the change in an organism's reactivity to the mediators of the vegetative nervous system and to narcotics during the period following acceleration confirms this idea.

We should note that there is agreement between the periods of time for recovering the glycogen content in the myocardium and the reactions to inhibitors of the vegetative nervous system.

The data which indicate a change in the functional interrelationships for the higher divisions of the central nervous system after accelerations were also obtained during a study of the reactivity to various narcotic substances [3, 11].

Thus, the results of the studies show that the pathogenesis of the breakdown in cardiac activity during transversely-directed accelerations is complex and involves changes in the biochemical process in the myocardium as well as in the functional interrelationships in the central nervous system.

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THE EFFECT OF LONG PERIODS OF TRANSVERSE ACCELERATIONS ON THE FUNCTIONAL STATE OF THE VEGETATIVE NERVOUS SYSTEM

V.Ye. Belay, P.V. Vasil'yev, and G.D. Glod

ABSTRACT: The effect of transverse accelerations on the vegetative nervous system was studied in experiments with rabbits and dogs, involving their reaction to adrenalin, acetylcholine, and electrical stimulation of the vagus nerve. It was established that within 15-20 min after the action of the accelerations, there is a change in the organism's reaction and an irritation of the vagus nerve. In this case, the length of time for individual orbits of the arterial pressure and the coronary blood flow are changed, as is the rate of heart contractions. The character of the reaction correlates with the degree of the disorders in cardiac activity during the action of accelerations and in the period following their application. The authors conclude that transverse accelerations change the functional state of the vegetative nervous system.

The effect of long-period, transversely-directed accelerations /124 on the functional state of various divisions of the vegetative nervous system in animals is studied in this article.

The studies were conducted on 43 dogs and 31 rabbits. Transversely-directed ("chest-back") accelerations were reproduced in a centrifuge with an arm 4.25 meters long. The magnitude of the effective acceleration was 12 units for the dogs and 9 units for the rabbits, with an acceleration and deceleration rate of 0.3-0.4 units/sec.

We determined the state of the vegetative nervous system by the animals' reaction to intravenous administration of adrenalin and acetylcholine, and also to electrical stimulation of the peripheral end of a transversely sectional vagus nerve. In careful experiments, the animals were anesthetized by intraperitoneal administration of a 10%-urethane solution in a dose of 2.0 g/kg. In the experiments, we recorded the electrocardiogram, the rate of respiration, the arterial pressure (direct method), and the relative level of coronary blood flow (according to the method of M.Ye. Marshak and G.N. Aronova [10]).

As the results have shown, the animals' individual sensitivity to the action of accelerations of a given value varies significantly.

During rotation in a centrifuge, regular changes were noted in the recorded physiological characteristics described by other authors [2, 8, 9].

The length of time required for this effect to lead to the appearance of signs showing a breakdown in cardiac activity varied within 1.5-40 min for the dogs and 3-32 min for the rabbits. The animals were subjected to the effect of accelerations both before the appearance of signs showing a "collapse" in the compensatory-adjusting reactions of the cardiac activity, and without such signs.

REACTION TO INTRAVENOUS ADMINISTRATION OF ADRENALIN /125

A freshly-prepared solution of adrenalin (1:20,000) was administered at a constant rate into the outermost vein of the rabbits' ears at a dose of 0.005 mg/kg and into the femoral veins of the dogs at a dose of 0.002 mg/kg.

The reaction to adrenalin differed greatly in different animals, but it was identical for a given animal during repeated administrations at intervals of 30-60 min.

The changes in the average level of the arterial pressure had the most informative significance. Reaction to the administration of adrenalin was characterized by the usual phase changes in the arterial pressure, which mainly showed increases [3]. In contrast to the control animals, the reaction to adrenalin for the animals which had been subjected to accelerations was unchanged. Moreover, the degree of change depended not only on the length of the after-effect period, but also on the degree of the disorders in cardiac activity during rotation in the centrifuge. For the animals which did not show signs of "collapse" in the compensatory-adjusting reactions of cardiac activity during accelerations, the changes in the nature of the arterial pressure reaction to adrenalin led only to an insignificant increase in the first pressor wave. More substantial shifts in the arterial pressure were observed after the accelerations, accompanied by definite disorders in cardiac activity (Table 1).

TABLE 1: PRINCIPAL SIGNS OF A CHANGE IN THE REACTION OF THE DOGS' ARTERIAL PRESSURE TO THE ADMINISTRATION OF ADRENALIN, WITHIN 15-20 MIN AFTER THE EFFECT OF AN ACCELERATION OF 12 UNITS, CAUSING A "COLLAPSE" IN COMPENSATION FOR CARDIAC ACTIVITY.

Change in the Reaction of the Arterial Pressure	Number of Cases	As a % of the Original Value
Lengthening of the Latent Period	7	58.3
Relative Dec. in the Pressor Comp.	10	83.4
Relative Inc. in the Depressor Comp.	8	66.6
Complete Disappearance of the Sec. Pressor Effect	3	25.0

-In the experiments on rabbits, the reaction of the arterial pressure to the administration of adrenalin after accelerations was characterized by a decrease of the pressor effect: these changes were greater with clear signs of "collapse" in compensation for cardiac activity during rotation in a centrifuge and lesser for a lack of these disorders. /126

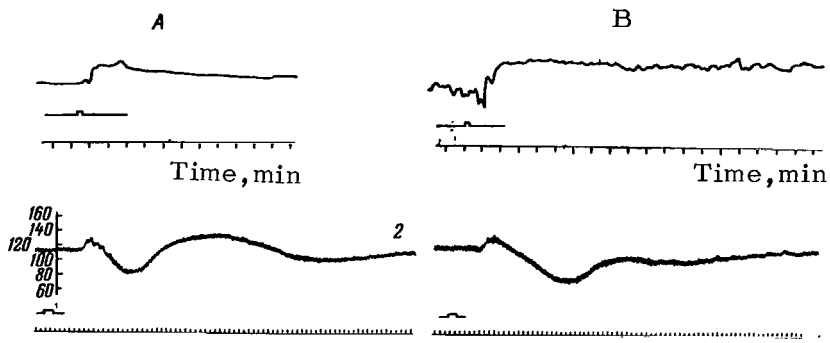

Fig. 1. Changes in the Coronary Blood Flow (1) and Arterial Pressure (2) of a Dog with Intravenous Administration of Adrenalin in a Dose of 0.002 mg/kg Before (A) and within 30 min After (B) the Effect of an Acceleration.

The changes in the rate of heart contractions varied within wide ranges. The degree of bradycardia, after the administration of adrenalin, agreed with the value for the increase in the arterial pressure, and this was observed for a brief time.

The data on the change in the relative level of the coronary blood flow are of particular interest. We know that adrenalin does not have a direct effect on the adrenergic systems of the coronary vessels, and the change in the level of the coronary blood flow after its administration was caused by general shifts in the hemodynamics and well as by changes in the metabolic process in the myocardium [4, 6, 11].

In our experiments, the reaction of the coronary blood flow to the administration of adrenalin, after the accelerations which were accompanied by a "collapse" in the compensation, greatly exceeded the amount of change during the control administration (Fig. 1). Following the accelerations which were not accompanied by disorders in the cardiac activity, the direction of the change in the reaction remained the same; however, the shifts were less pronounced. The data on the increase in the reactivity of the coronary blood flow to adrenalin during the period of the after-effects immediately following accelerations were also substantiated in chronic experiments on dogs.

REACTION TO INTRAVENOUS ADMINISTRATION OF ACETYLCHOLINE

A solution of acetylcholine, prepared *ex tempore*, was administered intravenously at a constant rate in doses of 0.05 (rabbits) and $0.48 \cdot 10^{-7}$ mg/kg (dogs). Within 15 min after the injection of acetylcholine, the electrocardiogram and the arterial pressure were recorded. Just as in the experiments with adrenalin, the nature of the reaction to acetylcholine differed in certain individual features. However, repeated injections of the preparation into a given animal, at intervals of 45-60 min, caused a stereotype reaction on the part of the physiological characteristics which were recorded. During the period of the after-effects immediately following accelerations (within 15-30 min), the differences in the amount of reaction for the arterial pressure were clearer (Table 2). /127

TABLE 2: CHANGES IN ARTERIAL PRESSURE FOR RABBITS (AS A PERCENT OF THE ORIGINAL LEVEL) FOR REPEATED ADMINISTRATIONS OF ACETYLCHOLINE.

Exper. No.	Char. of the Exper.	Time After Admin. of Acetylcholine, min.						
		0.5	1	2	3	5	10	15
185	Control	0.2	1.4	0.8	0.9	2.5	1.9	4.1
189	Control	0	1.9	0	1.8	1.0	0	0
181	After Accelerations.	8.5	6.5	13.3	19.3	30.8	14.8	5.2
210	After Accelerations.	2.8	0.8	0.2	6.5	4.6	4.6	2.0

As we can see from the data in Table 2, the degree and direction of the changes in the reactions of the arterial pressure in rabbits which had been subjected the effect of accelerations were different. In Experiment No. 181, a substantial difference in the value of the reaction was caused by a lesser depressor effect of acetylcholine following the accelerations, while in Experiment No. 210, repeated adminstration of the preparation caused (besides a one-minute reaction) a deeper hypotensive wave. The differences in the changes of the reactivity to acetylcholine in these experiments become understandable when we examine them in relation to the particular features of the animals' reaction to the effect of accelerations. Thus, in Experiment No. 181 the rabbit was subjected to the effect of an acceleration for 18.5 min; in this case, the rate of its heart contractions remained close to, or exceeded, the original level for up to 18 min, and bradycardia began to develop only at the end of the rotation. The maximum decrease in the pulse rate, toward the end of the action of the acceleration, was 62.5% of the original level.

In Experiment No. 210, the rabbit reacted in a different way to the effect of the accelerations: from the very beginning of the rotations, there was observed a decrease in the rate of heart contractions, which reached 46.7% of the original level toward the end

of the time for remaining on the "plateau". The total length of time for the acceleration effect in this experiment was 3 min.

The rate of heart contractions during the administration of /128
acetylcholine changed insignificantly; during the maximum decrease in the level of the arterial pressure, there was a slight reflex reaction, taking the form of an increase in the pulse rate by 1.8-3.7%.

In the experiments on dogs, the changes in the nature of their reaction to intravenous administration of acetylcholine, following accelerations which were accompanied by signs of "collapse" in the compensatory-adjusting reactions of the cardiac activity, were expressed to a lesser degree than in the rabbits, and were characterized mainly by a slower return of the level of the arterial pressure to its original value.

REACTION TO ELECTRICAL STIMULATION OF THE VAGUS NERVE

The rabbits' vagus nerves were stimulated by platinum-coated electrodes with the aid of the "Neurovar" instrument made by the "Alvar" firm, using square-wave pulses lasting 50 msec, at a repetition rate of 25 Hz. The length of time for stimulation was 5 sec, and the voltage of the signals was 10 V.

The data obtained have a rather high degree of reliability and show that there is a change in the reaction of the cardiovascular system to electrical stimulation of the vagus nerve during the period of the after-effects immediately following accelerations (Table 3).

TABLE 3: CHANGES IN RABBITS' ARTERIAL PRESSURE AND PULSE RATE (AS A PERCENT OF THE ORIGINAL) WITH STIMULATION OF THE VAGUS NERVE.

Characteristics	Statistical Index	Control	After an Acceleration of 9 Units	
			Within 10-13 min.	Within 60-120 min.
Max. Decrease in Arterial Pressure	n	19	8	9
	M	72,1	85,6	75,0
	$\pm m$	2,7	4,58	11,2
	t	—	2,55	0,24
Dec. in the Rate of Heart Contractions	n	20	11	12
	M	47,9	67,0	54,8
	$\pm m$	6,42	4,46	5,26
	t	—	2,45	0,83

The change in an organism's sensitivity to the vagal effects depended on the nature of the animals' reaction to the effect of accelerations and in particular on the degree of the disorders in cardiac activity during rotation in the centrifuge (Fig. 2).

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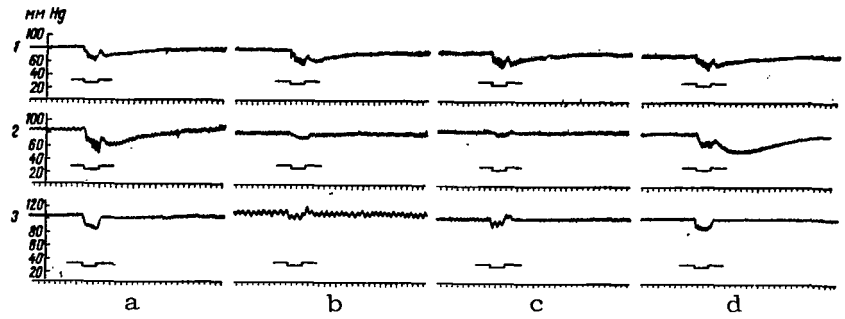

Fig. 2. Change in Rabbits' Arterial Pressure during Electrical Stimulation of the Vagus Nerve. From Top to Bottom: Arterial Pressure, Indication of Stimulation, Time Marker (2 sec). (1) Control Experiment; (2) Effect of Acceleration Without "Collapse" and (3) With "Collapse" of Compensation in Cardiac Activity; (a) Before Action of Acceleration; (b) 13-15 min After Acceleration; (c) 40 min After Acceleration; (d) 80 min After Acceleration.

As we can see from Figure 2, electrical stimulation of the peripheral end of the vagus nerve in rabbits was accompanied by a significant hypotensive wave. The general picture of the change had a clearly individual character (1a, 2a, 3a). However, in the control experiments (1a, 1b, 1c, 1d), there was a rather stable recurrence in each animal with repeated stimulations for 2 hours, a interval of not less than 15 min.

During the period of the after-effects immediately following the accelerations, the reaction of the arterial pressure to electrical stimulation of the nerve changed substantially. In experiments where there were no signs of a "collapse" in the compensatory and adjusting reactions of the cardiac activity during the 40-60 min following rotation in the centrifuge, the value for the reaction decreased sharply, and it acquired a character which was regular for a given animal (2a, 2b, 2c, 2d) only after 80 min. In the experiments which were accompanied by signs of "collapse", the changes in the nature of the arterial pressure reaction had the same direction, but there were also elements of inversion in the reaction: after the hypotensive phase, there was a second hypertensive wave (3a, 3b, 3c, 3d). We should note that similar interrelationships were observed in all the experiments for the nature of the change of the arterial pressure reaction to stimulation of the vagus nerve, and the differences consisted only in the degree of the changes.

DISCUSSION OF THE RESULTS OBTAINED

Thus, the results of the studies indicate that there are changes in the functional state of the vegetative regulatory centers during the period of the immediate after-effects for long-period, transversely-directed accelerations. In relation to this, we should /130 remember, in particular, that these shifts were detected rather clearly during normalization of the physiological characteristics, whose changes are generally accepted as indicating an organism's reaction to acceleration [2, 7].

The change in the reactions to adrenalin and acetylcholine show that the effect of accelerations is accompanied by shifts in the functional state of the sympathetic and parasympathetic divisions of the vegetative nervous system. In particular, the decrease in the pharmacological effect of adrenalin indicates considerable stress on the organism's sympathetic and adrenalin system. A.S. Barer [1] drew similar conclusions on the basis of his studies.

The value and direction of the change in the functional state of the vegetative nervous system during the effect of accelerations are governed, in our opinion, by a number of factors. The principal ones are the particular nature of the organism's reaction to an acceleration and, in particular, the degree of breakdown in the cardiac activity during the rotation. In fact, the reactivity of the animals to adrenalin and acetylcholine changes to a greater extent in those experiments which are accompanied by signs of "collapse" in the compensatory and adjusting mechanisms of the cardiovascular system. Another, no less important, factor determining the degree of the changes in the functional state of the vegetative nervous system is the length of time for the period of the after-effects. The greatest changes in reactivity are detected within 15-30 min after the accelerations, and then gradually level off; within 90-120 min, the organism's reaction acquires the character which is usual for its own individual features.

The varying direction of the change in the reactivity to the mediators of the vegetative nervous system, depending on the presence or absence of signs of "collapse" in the compensatory and adjusting mechanisms of cardiac activity, indicate that there are definite phases in the changes of the functional interrelationships among the vegetative regulatory centers. This assumption is also confirmed in the literature by materials on the phase changes of the bioelectric activity for the cortex and the subcortical formations of the cerebrum during the effect of transverse accelerations [5].

The experiments on rabbits, with administration of acetylcholine and stimulation of the vagus nerve, are of definite interest. During the intravenous administration of acetylcholine, the change in the reaction of the arterial pressure after accelerations can be in the same direction, depending on the degree of disorder in cardiac activity during rotation in a centrifuge. At the same time, the

experiments on electrical stimulation of the vagus nerve show that the changes in the reactivity of the cardiovascular system were directed unilaterally and depended on neither the presence or absence of signs of "collapse" in compensation for the cardiac activity. This difference can be explained, in our opinion, in the following way. /131 With intravenous administration of acetylcholine, the vascular component for regulating the arterial pressure has more unit weight, while the principal link in the development of the depressor reaction in electrical stimulation of the vagus nerve is the contraction of the rhythm for the cardiac activity. In fact, a comparison of the data on the value for the change in arterial pressure and pulse rate show that, in experiments with intravenous administration of acetylcholine, the rate of heart contractions is practically unchanged. At the same time, in the experiments with electrical stimulation of the vagus nerve, the hypotensive wave for the arterial pressure coincides with a lowering of the pulse rate. Actually, within 10-30 min following the acceleration, the depressor wave of the arterial pressure and the degree of bradycardia average 1.35 and 19.1% variation from the original level, respectively. This obviously indicates that the various links in the vegetative regulation of the cardiovascular system change their functional state under the influence of accelerations to various degrees.

Thus, the effect of transversely-directed accelerations is linked with a change in the functional state of the vegetative nervous system. The degree of these changes agrees with the severity of the disorders in cardiac activity, and this is preserved for 80-120 min after termination of rotation in a centrifuge. For accelerations which are accompanied by sharp disorders in cardiac activity, there is a functional overstrain on the sympathetic as well as parasympathetic divisions of the vegetative nervous system. This assumption conforms with the results of studies by A.S. Barer [1], who observed a decrease in the amount of adrenalin-like substances and acetylcholine in the blood of rats, even at accelerations of 10 units acting for 1 min. Obviously, the change in the functional state of the vegetative centers is one of the important links in the pathogenesis of disorders in the regulating mechanisms for blood circulation, occurring due to the effect of accelerations.

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MODELING THE FUNCTION OF REGULATION OF THE CARDIOVASCULAR SYSTEM DURING WEIGHTLESSNESS

I.I. Kas'yan and N.A. Chekhonadskiy

ABSTRACT: The problem of applying methods of mathematical modeling to a study of the function of the cardiovascular system is examined. Mathematical expressions and electrical circuits are presented for models which reflect the general rules for the function of this system under conditions on Earth and during weightlessness. The model obtained is used for examining particular features in the functioning of the cardiovascular system when carrying out physical work during weightlessness.

In examining the particular features in the functioning of the /132
cardiovascular system during weightlessness, we find it expedient to use the method of mathematical modeling, which is being applied more and more widely in biology and space medicine [2, 6].

Application of this method, as we know, is by no means an exhaustive procedure for studying the physiological process in itself, but it brings us closer to an understanding of certain parts of it, and it makes it easier to observe (to a certain degree) those rules (although very roughly) which would not have been noticed during regular experiments.

PRINCIPAL FEATURES OF A MODEL OF THE CARDIOVASCULAR SYSTEM

The cardiovascular system, in an examination of the most general regulatory processes, can be represented in the form of a mechanical model, as well as in the form of an electrical model. Such models are usually composed of a number of links which consider three principally different types of elements. In a mechanical model, this would be a certain mass, a spring, and an element of viscous friction.

The component elements of an electrical model are inductance, electrical capacitance, and resistance. In examining our problem, we will limit ourselves to a study of only the properties of a model which is made up of links of two types - inductance and resistance. The validity of using such a method comes from the following circumstances.

It is well known that, in imposing any functional physical stress, the rate of heart contractions increases. However, a

change in the pulse rate is made, not instantaneously, but after a definite period of time. Thus, the given process has a certain inertia, which is peculiar to the mass in the mechanical system, and peculiar to inductance in the electrical system. /133

The functioning of the cardiovascular system, naturally, involves energy expenditures. If we assume that each cardiac cycle is linked with expenditure of a definite portion of energy, then the increase in the pulse rate during physical stress, obviously caused a corresponding increase in non-recoverable losses of energy.

In a mechanical model, the non-recoverable losses of energy are reflected by the presence of an element of viscous friction, while, in the electrical model, they are reflected by resistance.

As a consequence, in studying the most general regulatory processes peculiar to the cardiovascular system during physical stress, we will use a very simple model which consists of such elements as inductance and resistance. Moreover, in order to abbreviate its name, we will in future call it the model of the cardiovascular system.

THE ELECTRICAL MODEL OF THE CARDIOVASCULAR SYSTEM UNDER THE CONDITIONS ON EARTH

The electrical models of the cardiovascular system, for an organism at rest and for a functional physical stress under the conditions on Earth are shown in Figure 1.

The inductance L reflects the presence of inertia in the system during an increase in the physical stress. The resistance R_0 reflects the presence of losses in energy during the resting condition of an organism, and the resistance R reflects an increase in the loss of energy caused by physical stress.

The presence at the input (Fig. 1a) of a voltage U_0 corresponding

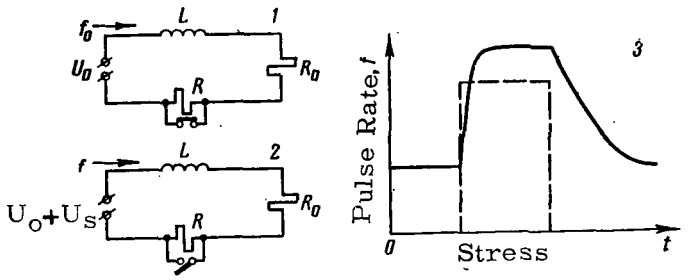

Fig. 1. Electrical Model of the Cardiovascular System Under the Conditions on Earth, and Its Dynamic Characteristic (1) Organism at Rest; (2) During Physical Stress; (3) Change in the Pulse Rate during Physical Stress

to a certain "stress" on the cardiovascular system when an organism is at rest causes a current connection, to which, in our case, the pulse rate f_0 corresponds. /134

In the case of the presence of physical stress (Fig. 1b) at the input, in addition to the voltage U_0, there is a voltage potential U_s, and the resistance R, which reflects the effect of a physical stress on the cardiovascular system, is switched on. The pulse rate in this case changes, and becomes equal to f.

Let us find the relationships between these values, deriving them from the properties of the electrical model for the cardiovascular system.

The pulse rate at rest is determined by the relationship:

$$f_0 = \frac{U_0}{R_0}. \tag{1}$$

During stress, the pulse rate reaches a value:

$$f_m = \frac{U_0 + U_s}{R_0 + R}. \tag{2}$$

The change in the pulse rate during measured physical stress for a certain length of time (Fig. 1c) will have the following character: the increase in the pulse rate during physical stress is the following:

$$f = f_0 + (f_m - f_0)\left(1 - l^{-\frac{t}{T_s}}\right), \tag{3}$$

where T_s is the constant for the time of increase in the pulse rate during stress; the recovery of the pulse rate after physical stress is the following:

$$f = f_m l^{-\frac{t}{T_{re}}} \tag{4}$$

where T_{re} is the time constant for the recovery of the pulse rate after the stress.

The time constant for an increase in the pulse rate during stress, T_s, is determined by the following relationship:

$$T_s = \frac{L}{R_0 + R}, \tag{5}$$

while during recovery of the pulse rate after the stress it is:

$$T_{re} = \frac{L}{R_0}. \qquad (6)$$

In analyzing (5) and (6), we can easily be convinced that

$$T_{re} > T_s.$$

Therefore, by using the very simple electrical model we have examined, which reflects the properties for regulation of the cardiovascular system during physical stress, we have the following features: /135

(a) The pulse rate increases in proportion to the stress.

(b) The increase in the pulse rate during measured physical stress occurs much more rapidly than does recovery after the stress.

The above-mentioned features of the electrical model reflect the general regulatory rules peculiar to the cardiovascular system during physical stress.

As an example which confirms this concept, one of the graphs for the change in the pulse rate in subjects exposed to 5 minutes of measured physical stress (according to the data of B.S. Katovskiy) is given in Figure 2.

In analyzing the materials presented, we can see that there is a certain feature of the human cardiovascular system which involves rearrangement of its parameters during the occurrence of physical stress.

The presence of this feature guarantees a more rapid return of the system to the necessary level for its functioning than would be the case if the system always had the same dynamic properties as those it has during the recovery of the pulse rate after a stress.

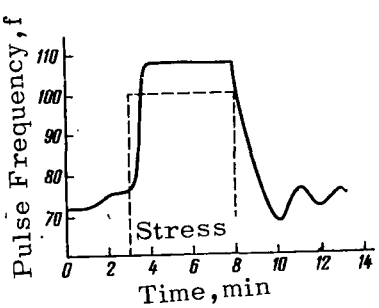

Fig. 2. Pulse Rate during Measured Physical Stress (According to the Data of B.S. KAtovskiy).

The degree of rearrangement for the regulatory system can be presented in the following way:

$$\beta = \frac{T_{re}}{T_s}. \qquad (7)$$

The concepts we have presented above relate to the functioning of the

cardiovascular system under the conditions on Earth. However, the same features are probably preserved, to some degree, during weightlessness.

Unfortunately, we do not now have enough materials on the reaction of the cardiovascular system to physical stress during weightlessness, which is of very great interest. Therefore, we attempted to analyze this problem by using the general properties of the above-described model for the cardiovascular system and the data we have on the character of the functioning of the cardiovascular system during weightlessness.

THE ELECTRICAL MODEL OF THE CARDIOVASCULAR SYSTEM FOR THE CONDITIONS OF WEIGHTLESSNESS

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In studies by V.N. Chernov and V.I. Yakovlev [8], O.G. Gazenko [4], R.M. Bayevskiy and O.G. Gazenko [1], I.I. Kas'yan and V.I. Kopanev [7], and V.I. Yazdovskiy et al. [9], it has been shown that the recovery of pulse rate in animals and humans during weightlessness occurs much more slowly than on Earth.

According to the data of A.R. Kotovskaya, normalization of the pulse rate for test subjects and astronauts after rotation in a centrifuge occurs within the first 3-5 min after termination of this effect. Under the conditions of weightlessness, the return of the pulse rate to its original values occurs after several hours.

Therefore, if we apply the model of the cardiovascular system to analyzing these data, we will see that the time constant for recovery of the pulse rate during weightlessness must exceed somewhat the analogous value under the conditions on Earth.

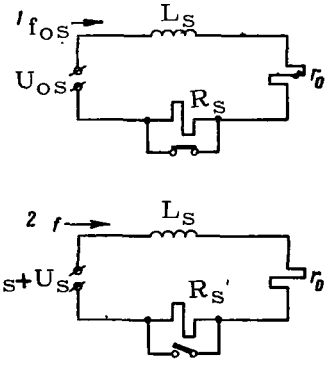

Fig. 3. Electrical Model of the Cardiovascular System During Weightlessness. (1) Resting Condition for the Organism; (2) Physical Stress

Moreover, the pulse rate for the majority of subjects at rest during weightlessness has a tendency to decrease somewhat, in comparison with the original values [1, 9].

The electrical models of the cardiovascular system, in a resting condition and with physical stress during weightlessness, are shown in Figure 3. The difference between the latter and similar models for the conditions on Earth consists in the following:

(a) The ohmic resistance for the model r_0 is less than the same value of R_0 for the conditions

on Earth, which reflects a decrease in the losses of energy for the functioning of the cardiovascular system during weightlessness;

(b) The voltage U_{0s}, guaranteeing the functioning of the cardiovascular system at a rate f_{0s}, is less than the same value for terrestrial conditions, as a result of which $f_{0s} < f_0$;

(c) The time constant for recovery of the pulse rate after physical stress $T_{re,s}$ is greater than the same value for terrestrial conditions.

Thus, this model of the cardiovascular system reflects the principal features of the functioning of the cardiovascular system during weightlessness.

CERTAIN FEATURES OF THE FUNCTIONING OF THE CARDIOVASCULAR /137

Using the properties of the model described, we will attempt to answer the question of what kind of reaction the cardiovascular system will show in response to physical stress during weightlessness.

One of the model's properties, as we have shown earlier, is the definite relationship between the time constant for the increase in pulse rate and that for its recovery after physical stress, expressed, by (7).

This relationship, which reflects the ranges for rearrangement of the cardiovascular system is probably also maintained during weightlessness, although it will be expressed numerically by another value.

Let us assume that the cardiovascular system during weightlessness has other ranges for the regulatory rearrangement than those on Earth.

We will represent this relationship in the following way:

$$n\beta = \frac{T_{re,s}}{T_{0s}} \qquad (8)$$

where T_{0s} and $T_{re.s}$ are the time constants for increase and recovery of the pulse rate for physical stress during weightlessness;
n is the range of adjustment of the cardiovascular system for physical stress during weightlessness.

The time constant for increase in pulse rate during weightlessness can be found from (8) in the following way:

$$T_{0s} = \frac{T_{re,s}}{n\beta} \qquad (9)$$

For terrestrial conditions, $n = 1$. The case when $n > 1$ corresponds to an increase; when $n < 1$, it corresponds to a decrease, in the range of adjustment of the cardiovascular system during physical stress under certain changed exterior conditions. Moreover, the increase in the latter (i.e. when $n > 1$) should be examined, in all probability, as a certain improvement of the dynamic properties of the regulatory system, while the opposite tendency indicates their decline.

Since the evolution of organisms on the Earth occurred during the presence of a constant force of gravitation, the various systems of these organisms function best under these same conditions (i.e., those to which they are accustomed). If deviations in either direction from the terrestrial conditions are permissible for certain organisms, then the processes of life activity will differ somewhat from the optimal ones peculiar to terrestrial conditions. As a result of this, in a number of the organism's systems (as we see it) there will be a certain change in the adaptation and compensation possibilities for the organism, primarily in the cardiovascular system. /138

On the basis of these assumptions, we will consider that under the conditions of weightlessness the range for readjustment of the cardiovascular system will decrease, i.e. $n < 1$.

In analyzing formula (9), we can easily see that this case corresponds to an increase in the time constant T_{0S}, in comparison with its value for terrestrial conditions.

The time constant T_{0S} can be represented in the following way:

$$T_{OS} = \frac{L_S}{R_S + r_0}, \qquad (10)$$

where L_S and R_S are the parameters of the electrical model of the cardiovascular system during weightlessness.

As follows from our hypothesis, there is a certain increase in the time constant T_{0S} during weightlessness. The latter can occur in the case when L_S increases, as well as in the case when R_S decreases. The first case is only slightly probable, since we have no reasons for anticipating any increase of inertia, determined in mechanical systems by the mass, during weightlessness.

Thus there remains the second case, i.e. the increase in the value of R_S corresponding to viscous friction, which causes non-recoverable losses of energy in the system.

Let us use the materials we have obtained for analyzing the particular features of the functioning of the cardiovascular system during weightlessness under repeated physical stress, with relatively

short-period intermissions in between. Figure 4 shows the curves for the change in the pulse rate during the time when a man is periodically performing physical work of a given intensity under terrestrial conditions and during weightlessness, constructed on the basis of the properties of our model. If, under terrestrial conditions, the relationship between the time for accomplishing the physical work and the pause is such that the pulse rate will not return to its original value, then this cannot occur under conditions of weightlessness.

Actually, such a parameter for the model of the cardiovascular system as R_s will not decrease under conditions of weightlessness. However, as follows from (2), a decrease in the latter during physical stress of the same intensity results in an increase of pulse rate.

Consequently, the level of the pulse rate will be higher during weightlessness than during accomplishment of similar work under terrestrial conditions.

Moreover, the recovery of the pulse rate to its original value the first time a man is under the conditions of weightlessness will occur much more slowly than on Earth.

Obviously, much more time is required for carrying our regular operations during weightlessness than on Earth. /139

This can lead to the fact that much more time is required for rest during weightlessness than is necessary when accomplishing similar physical work under terrestrial conditions (Fig. 4b).

The relationship between the time for rest during weightlessness t_{0w} and under terrestrial conditions $t_{0,te}$ should follow, as we are easily convinced, from the following dependence:

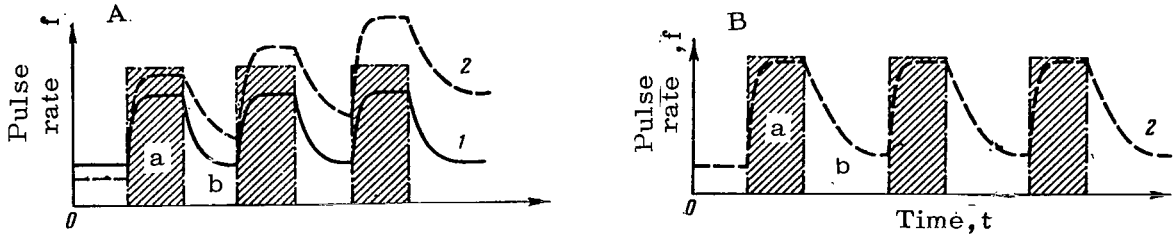

Fig. 4. The Pulse Rate under Terrestrial Conditions (1) and During Weightlessness (2) during Periodical Physical Work (a) of a Given Intensity and during Various Periods of Rest (b). (A) Length of Time for Rest in Weightlessness, Same as on Earth; (B) Length of Time for Rest During Weightlessness Increased.

$$t_{ow} \geq t_o, te \frac{T_{re,s}}{T_{re}} \qquad (11)$$

Such are the results leading from the properties of the model we have examined, which reflects to some degree the principal regulatory processes existing in the human cardiovascular system on Earth and during weightlessness. Further development of this problem, we can hope, will make the parameters of the model more accurate and, in particular, will allow us to study the possible adaptation of a human organism to the conditions of weightlessness as well as the individual features of the organism which affect the parameters of the model. This can permit using the model in /140 the future for a preliminary prediction of an organism's functional condition during weightlessness, which is of definite interest.

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REACTION OF THE HUMAN ORGANISM TO THE EFFECT OF RAPIDLY INCREASING ACCELERATION DURING LANDING

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ABSTRACT: The tolerance of a human subject to rapidly-increasing accelerations during landing, and certain ways for increasing resistance to them, are examined. The limits of good tolerance and the symptoms indicating an approach to these limits, as well as the nature of the changes in the functional systems of the organism are established. The maximum endurable accelerations were found to be those of 22-23 units, with a rate of increase of 4000-5000 units/sec acting for 0.03-0.04 sec in the "head-pelvis" direction and 35-40 units in the "chest-back" direction.

At the present time, in connection with the development of /140
rocket technology and space flights, a new problem has arisen in the domain of the study of limiting factors in space flights and their effect on the human organism - the problem of a safe landing for the crew in the spacecraft capsule.

It is well known that accelerations during landing differ substantially from accelerations during launching, in their rate of increase (more than 2000 units per second), length of time during which they act (hundredths of a second), and magnitude, and they can present significant danger to man.

Specific features of the events occurring during the landing process require special examination of the problem. The study of /141
the organism's responsive reactions to the effect of accelerations of great magnitude during landing, and the determination of human tolerance to them, are necessary conditions for guaranteeing successful space flights.

There are a large number of studies in world literature on the study of human tolerance to accelerations during landing [2-6].

However, a large number of questions in the landing problem, including the nature of its application, have been left unexplained. Thus for example, the question of the upper limit for human tolerance to accelerations during landing, and the question of ways for increasing resistance to them, have not been answered.

Solution of some of these questions has led in particular to the use of individually molded seats aboard the "Voskhod" spacecraft which guarantee the crew optimal conditions for tolerance to accelerations [1]. This article involves an examination of human tolerance to accelerations during landing, and the responsive reaction of the organism to such effects.

During the examination process, we conducted two series of experiments. In the first series, the direction of accelerations was close to the lengthwise axis of the body ("head-pelvis"). In the second series, transversely-directed accelerations predominated ("chest-back"). The landing was made on a special seat mounted on a platform, which was jettisoned onto soils of varying density. The accelerations were recorded on accelerometers which were mounted on the seat and platform.

An objective evaluation of the condition of the organism was made by a medical control group and by recordings of the electrocardiogram, the arterial pressure, ballistocardiograms, respiration, etc.

Ninety experiments in all were conducted, with the participation of 11 subjects.

For a homogenous distribution over the body of the pressure which arises at the moment of the appearance of the accelerations, and in order to increase human resistance to them, the seat was made up of individually shaped pieces of various synthetic materials. During the testing process, the accelerations increased gradually from experiment to experiment.

The limits for tolerance were determined by the appearance of adverse subjective sensations (pain, etc.) or by changes in the electrophysiological, clinical, and clinical and biochemical characteristics.

In the first series of experiments, unpleasant symptoms appeared in the form of pain in the area of the 4-5th thoracic vertebrae when the lengthwise component of accelerations reached 22 units. The time of the action of the accelerations in this series was within the range of 0.04 sec, and the rate of increase was 3000-4000 units/sec.

In the second series, accelerations on the order of 35 - 40 /142
units acting for 0.03 sec with a rate of increase on the order of 5000 units/sec were found to be close to the maximum that could be endured.

In this series, the appearance of pain in the pelvic region, and insignificant transitional changes in the subjects' urine (appearance of erythrocytes) was the moment which determined that further increase of the effect must be stopped.

In some experiments of the second series, we used a shock absorber, which decreased the accelerations in the head and chest areas by increasing the accelerations on the platform up to 70 units. In this case, the seat turned through an arc in the vertical plane at the moment of operation of the shock absorber. In view of the shortness of the turn, despite the significant angular accelerations (on the order of 300 units/sec^2), the maximum angular velocity was low.

In both examination series, the subjects evaluated the effect of the accelerations as an impact distributed evenly over the body and increasing in intensity with an increase in the magnitude of the active factors, all the way to the above-described pain sensations. There was also noted a significant predominance of individual modeling in comparison with the average (for a given age) modeling which was established in several control experiments. The subjects did not feel the seat turning.

The most typical changes in the objective characteristics did not exceed the limits for the physiological norm, and they were usual for such a type of action. These changes were observed mainly in the cardiovascular system. Thus, even immediately before the "discharge" (1-5 sec before), the pulse rate reached 110-115 beats/min. During the first few seconds afterwards, the pulse rate remained roughly on the same level, and it returned to its original value after 2-5 minutes (Fig. 1a).

In most of the subjects, there was a sinusoidal arrhythmia, linked with the phases of the respiration, beginning 30 sec afterwards.

An analysis of the electrocardiograms showed a definite relationship between the dynamics of the rate of heart contractions and the elements of the electrocardiograms. Thus, the *PQ* and *QT* intervals were shortened, with an increase in the rate of heart contractions, and they returned to their original values as the pulse slowed down. The systolic indicator (according to Fogel'son-Chernogorov) increased to 60-68% immediately before the beginning of the experiment; during the first seconds afterwards, it reached 65-78% and then gradually returned to its initial values (in 2-5 min). The *QRS* interval remained practically constant.

With an increase in the rate of heart contractions, the voltage of the T_{II} wave decreased, and it became flattened during the first few seconds. The voltage of the T_{II} wave returned to its original value about 20-30 sec afterwards. /143

Specific changes in the characteristics of the activity of the cardiovascular system were noted only in the experiments with effects which were close to marginal. Thus, in a number of cases, there was a slowing of the pulse from 120 (and sometimes even higher values) to 50-60 beats/min during the first few seconds of after-

effect (Fig. 1b). In these same experiments, there was sometimes a relative and even absolute decrease in the systolic and diastolic blood pressure from 130/65 to 80/30 mm Hg (Fig. 2).

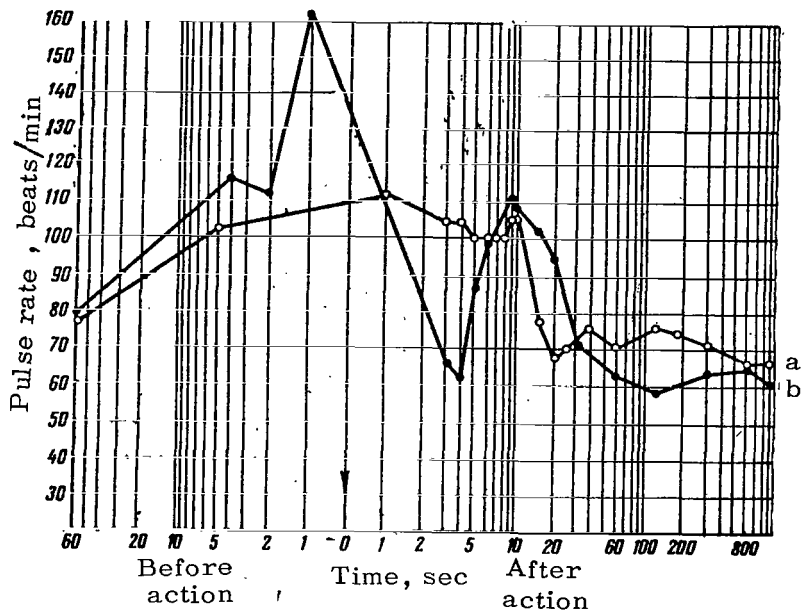

Fig. 1. Dynamics of the Rate of Heart Contractions for Subject D, during the Action of Accelerations with Values of 23 Units (a) and 39 Units (b) in the Direction "Chest-Back". The Arrow Shows the Moment of Action.

In the cases when there was bradycardia during the first few seconds of aftereffect, the *QT* interval remained shortened. The systolic indicator decreased by 7% during the moment when the rate of heart contractions was reduced. The *PQ* interval underwent the same changes as those described earlier.

These changes in the activity of the cardiovascular system can obviously be explained by the reflex effect on the part of the vagus nerve, and by the direct effect of accelerations on the coronary circulation.

In the dynamics of respiration for all the experiments, there /144
was a slight increase in rate immediately before the action, and a rapid return to the original values during the immediate aftereffect. In some cases, the increase in the respiration rate was maintained up to 3 - 4 minutes after the action.

Biochemical studies of the blood showed that there was an increase in the activity of the glutamine-asparagin and glutamine-alanine transaminases during the effect of accelerations which

are close to the limit for good tolerance.

In the neurological picture, there was a uniform activation of the tendinous reflexes in a number of experiments during the aftereffects, which should be viewed as the result of emotional stress.

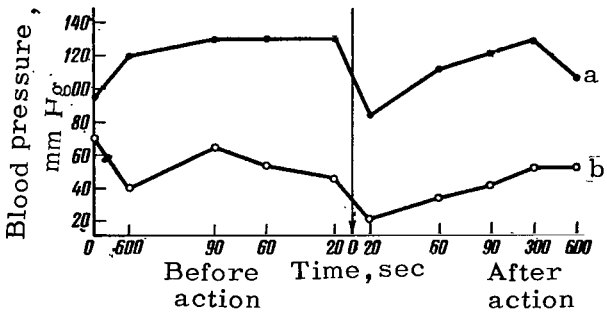

Fig. 2. Dynamics of Arterial Pressure for Subject during the Effect of an Acceleration of 23 Units in the Direction "Head-Pelvis". The Arrow shows the Moment of the Effect. (a) and (b) are the Systolic and Diastolic Pressures.

There were no coordinative and vestibular disorders noted, even in the experiments where angular accelerations occurred.

CONCLUSIONS

(1) Accelerations during landing, at a rate of increase on the order of 4000-5000 units/sec and an effective time of 0.03-0.04 sec, were found to be endurable by humans within the range of 22-23 units when their action is in the direction "head-pelvis", and within the range of 35-40 units when they acted in the direction "chest-back".

(2) Of the numerous symptoms studied, the principal ones indicating that the accelerations during landing are close to the tolerance limit are pain sensations in the area of the thoracic vertebrae and changes in the activity of internal organs: bradycardia and a decrease in the arterial pressure as aftereffects, the appearance of fresh erythrocytes in the urine, and an increase in /145 the activity of the glutamine-alanine and glutamine-asparagin transaminases for the blood.

(3) Individual modeling is an effective means of increasing human resistance to accelerations during landing.

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EFFECT ON MAN PRODUCED BY ACCELERATION DURING LANDING IN A CABIN, DEPENDING ON THE DEGREE OF SHOCK ABSORPTION AND THE FORCE OF HORIZONTAL WINDS

G.P. Mirolyubov, N.I. Frolov, and V.B. Lemasov

ABSTRACT: The conditions for landing in a cabin are examined in this article as depending on the damping properties of the shock absorbers, the position of the subject in the seat, and the velocity of the wind drift. The shock absorber, which damps the impact evenly and rapidly, guarantees a safe landing for the subject in the cabin in a sitting or semi-reclining position at a velocity of vertical descent of 20 m/sec, with a minimum braking rate of 8 m/sec. Landing in the cabin during wind drift is accompanied by accelerations whose components have vertical and horizontal directions. With an increase in the velocity of the wind drift, the vertical component increases. The subjects' greater resistance to accelerations in the directions "chest-back" and "back-chest" provide a basis on which the introduction of a manual or automatic turning of the cabin, in order to increase landing safety, is recommended.

Landing directly in a cabin is one of the most reliable methods /145 for recovering the crew from a space flight. A cabin significantly improves the protection of the astronauts from the extremal factors of high altitudes and flight velocities, and it helps to save them in case of an accidental landing in an uninhabited locality.

These advantages were considered in selecting the methods for landing the crews of the spacecraft. In the USA, the technique of "splashdown" is used, with special shock absorbers which damp the impact and decrease the accelerations. In the Soviet Union, a soft-landing technique is used.

In the case of a breakdown in the soft-landing system, or in landing the cabin under the conditions of a strong wind, hard ground, rugged terrain, etc., there can be accelerations which present danger to humans at the moment of the impact.

Considering the possibility of using damping devices in the case of a dangerous (accidental) landing, we see the urgency of the problem of studying the safety of landing for a man in a cabin which

is equipped with a shock absorber. In previous experiments on animals, high effectiveness was obtained by using shock absorbers with a relatively low damping rate [1]. This article involves similar studies with human subjects.

METHODS

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Twenty-six subjects, ranging in age from 25 to 35, participated in the experiments. 220 experiments in all were conducted, divided into 12 series.

The value of the damping rate of the shock absorbers used, the velocity of the wind drift, and the position the subject assumed in the cabin were analyzed.

In the experiments, we used certain types of shock absorbers which varied in damping value during the landing impact. The examinations were conducted in a model cabin with a seat tilted back 20° (sitting position) and 60° (semi-reclining position).

In the model cabin with the seat tilted at 20°, experiments were conducted which dealt with a sideways landing at an angle of 45° to the left and right of horizontal.

The landing of the cabin under calm weather conditions was made on an immobile tower-test bed. Landing in a wind drift was imitated on a test bed which moved at a rate of 36 km/hour.

In order to determine the tolerance to the impact of accelerations for the subjects during 10-15 min (including the moment for action of an acceleration), we recorded the arterial pressure, the electrocardiogram in the standard intervals I and III, and the rate of respiratory movements. During the same period, we recorded the length of time for the latent period of a motor-response reaction to mild stimulus, and we determined the level of the conditioned reflex with time.

During the clinical studies made 30 min after the landing, we conducted functional tests with stresses on the cardiovascular system. In addition, the subjects were interrogated briefly on their feelings and on particular features of the experiment which they noted. A change in the subject's position at the moment of the effect of an acceleration was recorded with the aid of high-speed photography (900 frames per second). An x-ray examination of the spine was made according to the indications.

RESULTS OF THE STUDIES

In the first group of experiments, we studied the relative tolerance to accelerations on landing at a vertical rate of descent as a function of the damping rate, with the subjects in a semi-reclining position (Table 1).

Damping of the cabin at a high rate guarantees a safe landing for a vertical rate of descent of 10 m/sec. With a decrease in the damping rate by 5-7 times, the permissible velocity decreases to 7-8 m/sec.

With a decrease in the operation of the shock absorber, the acceleration increases; in relation to this, the subjective data indicating a decline in tolerance also increase. Thus, the opinions, of the subjects who took part in the experiments of the 3rd and 4th series were more emotional. In this case, a rigorous impact distributed over the entire body, brief headaches, and disagreeable sensations in the chest and peritoneal cavity were most frequently noted. /147

TABLE 1: EXAMINATION OF THE SUBJECTS' TOLERANCE TO ACCELERATIONS DURING LANDING IN THE CABIN WITH A VERTICAL RATE OF DESCENT AS A FUNCTION OF THE TYPE OF SHOCK ABSORBER AND THE DAMPING RATE (SPACE FACTOR OF THE DIAGRAMS).

Type of Shock Absorber	Max. Rate of Descent m/sec.	Max. Acceleration of Landing, Units	Space Factor of the Diag., marks	No. of Exper. Cond.	No. of Subj. Tested
Large Air-Flow	10	30	+	35	16
Large Cellular	10	12	+++	18	12
Small Air-Flow	7	20	+	18	2
Small Mechanical	8	45	++	43	6

It was noted that, in addition to the quantitative aspect of the nature of the damping, there was also a qualitative aspect which effected the tolerance to accelerations. This was the uniformity of the damping.

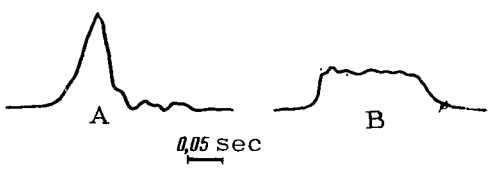

Fig. 1. Graph of Accelerations with Various Space Factors of the Diagram for a Shock Absorber of the Type "Large Air-Flow" (A) and the Type "Large Cellular" (B).

For uniform damping, which is achieved by using a shock absorber which has a high space factor for the diagram, the energy of the impact is dissipated throughout the entire duration of deceleration. The acceleration occuring in this case is smaller in value, and it takes on a characteristic trapezoidal shape (Fig. 1). We thus consider that the shock absorber which has the greatest damping rate and the greatest space factor of the /148

diagrams to be the optimal one.

In the second group of experiments, we examined the effect of the subject's position on tolerance to impact with during landing (Table 2).

TABLE 2: EFFECT OF SUBJECT'S POSITION ON TOLERANCE TO ACCELERATIONS DURING LANDING AT A VERTICAL RATE OF DESCENT*.

Subj. Position	Max. Rate of Descent, m/sec	Max. Accelerations during Landing Units	No of Exper.	No. of Subj.
Sitting	9.6	29.6	56	19
Semi-reclining	10	30	35	16
On the Right Side	7	15	12	2
On the Left Side	7	15	12	2

*We Used a Shock Absorber of the "large air-flow" type.

From articles dealing with pilot ejection, we know that one of the indicators of good tolerance to accelerations is the preservation of the subject's original position. The more the head deviates to one side, or the body moves (as observed in the subject), the greater the danger of traumatization.

According to the results from the filmed materials, the most advantageous position for the subjects in the cabin during landing at a vertical rate of descent is the semi-reclining position.

In the semi-reclining position, the subjects' heads moved less, as did their bodies. For the same force of the effect, but with the subject in a sitting position (Table 2, Sixth Series), the head moved 2-3 times as much. At the same time, we noted that the upper brachial zone moved downward several centimeters, which, in some experiments, was accompanied by a feeling of pain in the cervical or thoracic region of the spine.

The outcome of the experiment for a sitting position, in comparison with a semi-reclining position, depended greatly on the care with which the seat belts were attached.

With the subject on his side, his body made oscillating movements "down-up-down", with attenuation of the amplitude, at the moment of landing. With reinforcement of the belt system by additional lateral belts, the movements of the body decreased, which permitted experiments at accelerations of 15 - 16 units during landing of the cabin at a velocity of 7 m/sec.

Obviously, convenient lateral supports for the seat can increase human tolerance (with the subject on his side) to high accelerations during landing at a rate of 9 - 10 m/sec. It is important to consider this condition since, in practice, landing in a cabin does not eliminate impact from the lateral surface or its wind drift in the lateral direction. /149

The subjects' expressions of their feelings correspond to the results of objective observations. Accelerations were endured more easily by those subjects who were in a semi-reclining position. Accelerations of the same value for a sitting position, and of much lesser values for a position on one's side, caused disagreeable sensations and even algesic symptoms.

An examination of the conditions for landing with imitation of wind drift (the third group of experiments) was made in the cabin, where the subjects were placed in a sitting position facing forward, backward, or sideways according to the direction of motion (Table 3).

TABLE 3: MAXIMUM ACCELERATIONS ENDURABLE BY SUBJECTS IN THE CABIN, WITH A VERTICAL RATE OF DESCENT OF 7 M/SEC, FOR SIMULTANEOUS WIND DRIFT OF 8-10 M/SEC.

Direc. of Wind Drift	Maximum Acceleration, units		Number	
	Vertical	Horizontal	of Exper.	of Subj.
Forward	19	9	10	4
Backward	19	9.6	6	4
To the Right	24	10.3	6	2
To the Left	25	11	4	2

After the cabin left the test-bed, it fell (not perpendicularly, but at an angle to the horizon) and skidded along the ground after landing. The acceleration produced was also directed at an angle to the horizon and consisted of vertical and horizontal components.

With an increase in the velocity of the wind drift for the cabin, the component for the vertical direction showed the greatest increase, while that for the horizontal direction remained approximately constant.

Thus, an increase in the rate of drift is limited by the value for the acceleration in the "head-pelvis" direction. However, the direction of drift in relation to the subject is of great significance.

From the point of view of subjective sensations, we can consider the drift of the cabin with the subject facing backward or forward to be the most advantageous. In both cases, the horizontal component

of the accelerations acts in the sagittal plane "back-chest" or "chest-back". The body then has a support which limits its movement under the effect of acceleration. In the first case, this is seatback fitted with a headrest; in the second case, it is additional belts. /150

Landing with drift of the cabin in the direction in which those inside are facing forward differed somewhat in that there was a greater deviation of the head. On the basis of this, we can assume that with an increase in the acceleration in this direction (for example, with another shock-absorber system), the most advantageous direction is that of a drift of the cabin with the subjects facing backward.

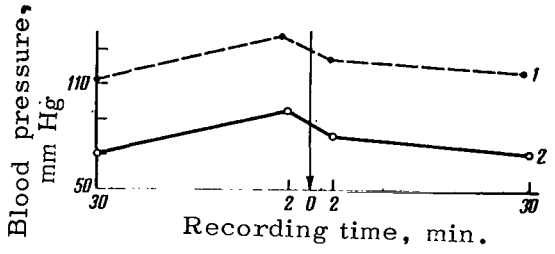

Fig. 2. Maximum (1) and Minimum (2) Arterial Pressure in Subjects during the Effect of Accelerations on Landing. The Arrow Indicates the Moment of the Effect.

Landing in a cabin with a drift in the lateral direction, when the horizontal component of the acceleration acts from side to side in the frontal plane was sometimes accompanied by disagreeable sensations caused by a sharp movement of the subject's head and body to the side.

For an acceleration of a small value, this was eliminated by a raised edge on the side of the headrest and seat, and by additional lateral belts.

Nevertheless, from the materials of the experiments we can conclude that the lateral direction for the drift of the landing cabin is less advantageous for the crew.

The changes in the functional activity of the organism in response to the effect of acceleration during landing were similar in all the series of experiments. The respiration rate, pulse rate, and value for the arterial pressure increased toward the moment of imminent accelerations. The maximum values for these characteristics were reached immediately before and after the landing; they then gradually decreased in about 2 or 3 minutes to their original values (Fig. 2).

The results of the tests with functional stresses on the cardiovascular system, conducted 30 min after the landing, were practically the same as in the controls.

The time for the latent period of a responsive motor reaction for the subjects varied from 0.17 to 0.25 sec, which does not exceed the limits observed in healthy subjects during measurements under laboratory conditions. After the landing, it changed (in /151

comparison to the background data) by an insignificant value which had practically no meaning.

The conditioned reflex also remained constant during the time after the action. Moreover, after the landing, the subjects in most of the experiments noted this time with great accuracy, even before the effect of the acceleration of collision.

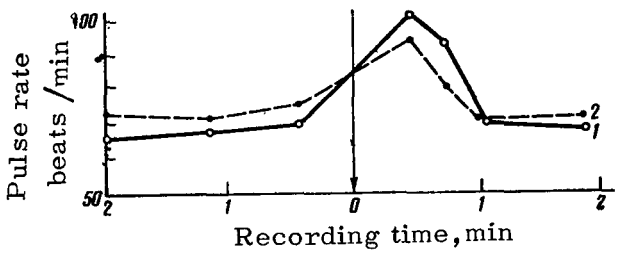

Fig. 3. Pulse Rate for a Subject in the Control (1) and Regular (2) Experiments. The Arrow Indicates the Moment of the Effect.

The results of studying the reaction of the cardiovascular system, respiration, and changes in the motor areas indicate that they did not depend on the accelerations during landing in the experiments we conducted. The changes noted were caused by emotional stress alone.

This assumption is confirmed by the results of the control experiments, in which the action of an acceleration was eliminated in preserving the emotional factor (the general situation of the experiment, the launching of the cabin, the commands to land, etc.). The pulse rate recorded for one subject in a control experiment was similar to the rate observed in an experiment with the effect of an acceleration (Fig. 3). As we can see from Figure 3, despite the lack of an acceleration, the responsive reaction of the organism appeared as an increase in cardiac activity (to a large extent).

After the effect of acceleration on subjects in a sideways position, there was a deviation in the electrical midline of their hearts. Considering similar data obtained in experiments on animals, accompanied by movements of the heart in the chest (confirmed by x-rays), we can assume that the deviation of the electrical midline of the heart in the subjects was also related to the effect of acceleration [2] on landing. /152

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THE PROBLEM OF DISORDERS IN LOCAL BLOOD CIRCULATION IN MAN DURING PROLONGED TRANSVERSELY-DIRECTED ACCELERATION[1]

M.D. Yemel'yanov and E.S. Kotova

ABSTRACT: The results of studying the retinal blood circulation are presented; it is shown that the retinal arteries can reflect both the condition of the local blood circulation in the eye and changes in the hemodynamics of the brain. The blood circulation was studied during the action of accelerations of various degrees. The authors state their opinion that only a comprehensive and detailed examination of the mechanism for the disorders in the hymodynamics during accelerations can solve the problems regarding rational regimes for preparing and training a special crew.

Numerous studies have treated the problem of the effect produced in an organism by prolonged acceleration, in relation to the conditions aboard a space flight [1,5,7,11]. /152

However, the essential questions related to the tolerance to repeated acceleration, the significance of training, the effect of transition from acceleration to weightlessness and vice versa, etc., still remain unexplained. Obviously, this circumstance is due to the difficulty in imitating the conditions aboard a space craft on Earth, and by a lack of fairly reliable criteria for evaluating previous disadvantageous physiological shifts in the human organism.

In relation to this, the hemorrhaging in the internal organs of animals, described by A. Holl and I. Mosely, which can occur even at moderate values of acceleration and, at the same time, are not diagnosed under regular examination conditions [10], naturally attracts our attention. It is well known that some of the principal physiological factors limiting tolerance to acceleration are the changes in the cardiovascular system [3, 6]. Loss of consciousness and energy losses depend on these very disorders in the blood supply to the brain and the eyes.

Under these conditions, the study of retinal blood circulation

[1]Article presented at the XVIth International Astronautical Congress. Athens, September 13-18, 1965.

acquires very great significance, both for understanding the mechanism of the local processes in the eye, leading to a loss of peripheral and central vision, and for determining the changes in the system of carotid blood circulation [2, 4, 8, 12]. The authors are convinced that the retinal arteries reflect the changes in the cerebral vessels and the intracranial pressure. Actually, the phylogenetic unit consisting of the eyes and brain and their vessels permits determining the condition of the blood circulation in the brain according to the retinal blood circulation. All the changes which we are observing reflect intracranial vascular shifts. /153

Taking what we have described into account, we included the following in our method: ophthalmodynamometry, campimetric examinations of the blind spot with an angioscope, and also the usual clinical determination of visual acuity, accomodation, etc.

Ophthalmodynamometry is a method which very carefully determines the origin of the different changes in the system of the internal carotid artery. A comparison between the retinal and general arterial pressures permits evaluating the intracranial pressure.

The conditions of the vessels in the conjunctiva of the eyeball, the episclera, and the retina were determined with the aid of color photography.

All the examinations were conducted under dynamic conditions, beginning with the first minute after stopping the centrifuge (the immediate aftereffects) and before complete recovery of the functions.

We assumed that the use of this combination of methods for ophthalmological studies allows detection of the earliest signs of hemodynamic changes particularly in the system of blood flow in the brain, and produces additional data for determining the dynamics of the subsequent reactions in the cardiovascular system during accelerations.

Several series of experiments were conducted, in which human subjects were used. We used accelerations acting in various directions and ranging from insignificant to the maximum endurable in value and length of time. In this case, particular attention was given to repeated accelerations.

The examinations revealed very regular reactions, involving phase changes in the vascular tonus, mainly the diastolic pressure and the diameter of the retinal arteries and veins.

During the immediate aftereffects, we determined the hypertension in the orbital artery, which had a pronounced regional character as did its changing hypotension. The retinal-brachial index changed pathologically. With an increase in the qualitative changes, there was a clear regularity during the effect of accel-

erations up to 14 g. At higher values, individual differences were clearly evident.

In contrast to the generally accepted opinion that all the functions recover rapidly after the effect of accelerating forces, we found residual reactions in the form of an expansion of the diameter of the retinal veins to 170 μ (for a corresponding norm, according to age, of 125-155 μ) 5, 8, and 11 days after the experiment. /154

The discovery of hemmorhages in the conjunctiva of the eyelids, eyeballs, and retinal membrane also proved to be a very important observation. Dynamic observations revealed the various origins of their formation. Together with hemorrhages occurring sometimes within the first 12-100 min after acceleration, significant hemorrhaging appeared for some of the subjects within 24-35 hours after the experiment, along the path of the major retinal vessels.

In 1954, Duane [9] first described the changes in the retinal vessels during positive transversely-directed accelerations. Duane, Lambert, Wood, and others found that the disappearance of vision ("blackout") during accelerations is a retinal-ischemic phenomenon. However, the results of these studies were obviously based on visual observations during the time of acceleration and the period immediately following.

Our examinations allow developing and supplementing these concepts. In all probability, the disappearance of vision (blackout) occurs earlier than loss of consciousness only because the retinal membrane is made of tissue which is more sensitive to anoxia. It is very probable that the local hypertension noted in our studies is a resistant reaction during the period immediately following stress, and is a factor of great significance in surmounting the resistance of the collateral circulation under the conditions of recovery of the blood circulation in the brain.

We can also assume that the arterial pressure increases during the deceleration period of the centrifuge. One of the observations which confirm this concept is the recovery, during the "landing" period, of peripheral and central vision, even at the beginning or middle of deceleration.

There is no doubt that detailed study must be devoted to the mechanism of the reactions in the blood circulation in order to solve the problems of forming rational regimes for preparing and training the special crew. The study of the recovery period after the effect of accelerations also provides more correct evaluation of the shifts which can occur in the astronaut's organism under the conditions of weightlessness when the craft is passing through dense layers in the atmosphere.

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PROBLEM OF THE ORIGIN OF OPTIC DISORDERS DURING ACCELERATION

B.M. Savin

ABSTRACT: The functional condition of the optic analyzer is examined during the effect of accelerations. It was shown that accelerations have a significant effect, both on the spontaneous bioelectric activity of various divisions of the optic analyzer, and on the course of phenomena related to the action of adequate stimuli. The results of the studies show the cortico-retinal nature of the disorders observed.

Clear evidence of breakdown in the activity of the central nervous system during acceleration is given by disorders in the function of the optic analyzer [1, 4, 8, 15, 27, 28, 29]. Although the symptomatology and the particular features of the development of optic disorders in relation to the value and the vector of an acceleration are now being studied in rather great detail [3, 11, 16, 17, 30], much still remains unclear and debatable with regard to the mechanism of their origin. Some authors link the breakdowns in vision to disorders in the retinal [2, 9, 24, 26, 29, 36] or cerebral [12, 13, 14, 22, 23, 32, 33] blood circulation alone. Others [7, 10, 35] see the cause in the appearance of unusual afferent stimulations in the central nervous system, causing retardation in the area of the cortical division of the analyzer by the mechanism of negative induction. Finally, a third group explains their appearance by purely mechanical phenomena: the eyelids covering the pupils [5, 6, 20, 30], changes in the shape of the eyeball, deformation of the eyes' optical media [21, 34, 35], difficulty in the flow of the lacrymal fluid, appearances of esophoria as a result of a breakdown in the equilibrium of the eye's muscular system [31], and also the movements of the eyeball in the orbit as a consequence of the noncoincidence of its center of gravity with the center of rotation. /155

Until rather recently, the evaluation of the shifts in the functional condition of the optic analyzer was based mainly on the data of subjective indications. Only very recently have we been using objective methods - in particular, ophthalmography of the fundus oculi [18, 19], electroretinography (ERG) [25], and analysis of the photic elements in electrocardiography (ECG) [11, 19, 23].

In our studies, in order to obtain more complete information on the change in the functional state of the optic analyzer during the effect of acceleration, we used the method of induced potentials together with an ERG recording. /156

All the examinations were conducted in chronic experiments on unanesthetized cats. We recorded the electroretinograms(ERG) and the primary responses(PR) of the external corpus geniculatum, the upper tubercles of the lamina quadrigemina, and the visual cortex.

The bioelectric potentials of the retina were determined with the aid of implanted electrodes, one of which was connected to the nasal bone at the medial margin of the pupils, and the other was connected to the zygomatic branch of the temporal bone.

For stimulation we used flashes of white light lasting 1 msec, with an energy of 0.6 J, occurring as a series of pulses. The distance from the flash lamp of the photostimulator to the animals' eyes was equal to 420 cm. During the experiment, the animal was kept in darkness. Before putting the animal in a container in the centrifuge, we atropinized its eyes and immobilized the eyelids: We used monopolar and bipolar recording.

In order to produce acceleration, we used a centrifuge with an arm 4 meters long.

The magnitude of the accelerations ranged from 1.5 to 22 units, lasting from 20 to 120 sec.

The ERG and the PR were recorded before the effect of the acceleration, at the very moment of its application, and during various periods afterwards.

Constancy of the intensity of the light stimulus during the period of rotation in the centrifuge was guaranteed by using a special device which provided for automatic transmission of the light pulses timed with the revolutions of the centrifuge at the moment the animal's body passed through a given point in the rotation plane. When the animal was at a given point, the direction of the light flux coincided with the optical axis of the eye.

The experimental data were developed by sequential integration of the amplitude value for the electric potential of each of the responses for a series, at a fixed time after the moment of the action of the light stimulus. In analyzing the experimental data, we considered the latent periods of the responses, the value (amplitude) and duration for the components comprising the response, and also the form of the responses themselves. For the principal characteristic of the functional condition for the corresponding division of the analyzer, we took the latent period of the "*B*" wave in the electroretinograph and the positive phases of the PR for the external corpus geniculatum and the visual cortex.

As the examinations showed, the accelerations have a significant effect on the spontaneous bioelectric activity of various divi- /157
sions of the optic analyzer, as well as on the course of electrical phenomena related to the action of adequate stimuli or afferents. The nature of the changes and their significance varied with the value of the acceleration and its recurrence.

For the single action of accelerations with small values (up to 5 units), it is primarily the electrical responses of the retina and the visual cortex which change. A characteristic change in the ERG is a decrease in the "*B*" wave, which is observed almost from the very beginning of the effect.

It appears possible to distinguish two phases in the changes of the PR for the visual cortex. At the beginning of the effect, we find a small increase in the amplitude of the positive as well as negative phases of the response. Subsequently, together with an almost complete disappearance of the negative phase, there is observed a significant weakening of the positive component as well.

It is not so much a change in the excitability of the corresponding cortical elements as a shortening of the time for the reaction of specific thalamic formations which forms the basis of the limited reduction of the latent period for the responses of the visual cortex. The shortening of the latent periods for the responses of the external corpus geniculatum indicate this.

For a single effect of accelerations with average values (from 5 - 12 units), or for the repeated effect of accelerations with values of 4-5 units, the ERG and the PR of the visual cortex change more sharply. In this case, in addition to the significant weakening of the amplitude for the responses, their latent periods are observed at greater intervals. This related primarily to the responses of the retina and the visual cortex. As for the responses of the external corpus geniculatum, despite the fact that their latent periods also increase, the difference between them and the latent periods for the responses of the retina decreases. The latter circumstance shows that, in addition to the intensification of the inhibition processes in the retina and the cortical region of the analyzer, specific thalamic formations are in a state of increased excitation during this time.

Averaged data, as shown in Figure 1, represent the nature of the changes in the ERG and the PR of the visual cortex during a single effect of acceleration with values of 6 and 12 units. We can see from the figure that the effect of acceleration of a relatively small value(6 units) caused a significant change in the form and the amplitude of the electric responses(Curve B). Both the positive and negative phases of the responses decreased. The curve for the rise and fall of the potentials became more extended in time. However, the latent periods of the "*B*" wave in the ERG, and of the positive phase of the PR for the visual cortex, did not change in this case.

A very different pattern was observed for changes during the action of an acceleration with a value of 12 units (Curve D). In this case, together with a sharp decrease in the amplitude of the re-/158 sponses, there was a significant lengthening of the latent periods, based on an increase in the latent periods for responses of the retina.

During the period immediately following accelerations (Curves C and D), latent periods of the responses did not differ from the original ones. As for their amplitude, both the positive and the nega-

tive phases of the responses continued to decrease during this time.

The ERG and the PR change even more sharply during the action of accelerations which are close to the maximum endurable value. The responses of the visual cortex were frequently suppressed completely in this case. Its spontaneous activity also discontinued. In such a case, when the responses of the visual cortex to the effect of specfic afferents are nevertheless preserved, their latent period increases very sharply. The latent periods for the responses of the external corpus geniculatum changed rather insignificantly in this case, which indicates a development of the retardation processes, primarily in the cortical division of the analyzer and in the retina.

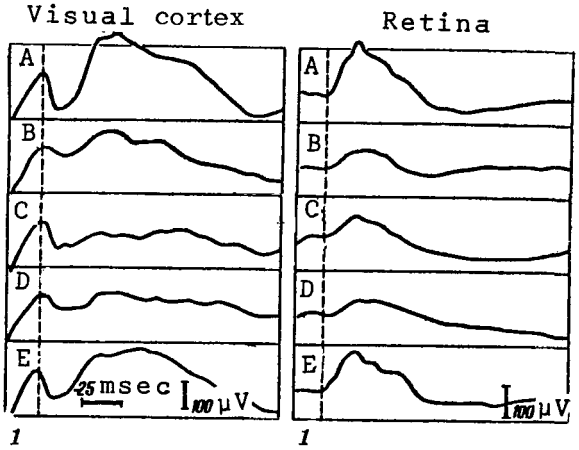

Fig. 1. Change in the Electrical Responses of the Retina and Visual Cortex during Acceleration in the Direction "Head-Pelvis" (Averaged Data). The Deviation of the Curves Downward Corresponds to an Increase in the Positive Potential in the Response of the Visual Cortex, and to an Increase in the Negative Potential in the Response of the Retina. (1) Latent Period of Response Before Acceleration; (A) Electric Response Before an Acceleration; (B) During an Acceleration of 6 units; (C) During the Period Immediately Following; (D) During an Acceleration of 12 Units; (E) During the Period Immediately Following.

During the repeated action of Accelerations which are close in value to the maximum endurable, together with a complete suppression of the responses for the visual cortex, there were often observed cases when the responses of the external corpus geniculatum were greatly weakened. In this case, despite significant weakening of the response of the upper tubercles, its retention indicates /159 that the capacity of the retina to receive adequate stimulation is not completely exhausted during this time.

According to the particular features of the changes in the ERG and the PR of various divisions of the optic analyzer, all the experiments were divided into 3 groups. The first group showed the effect of accelerations ranging from 1.5 - 5 units, the second group from 5.1-12 units, and the third group from 12.1-22 units. The results of the statistical analysis are shown in the table.

CHANGE IN THE LATENT PERIODS OF THE ERG AND THE PR FOR THE EXTERNAL CORPUS GENICULATUM AND VISUAL CORTEX, AS A FUNCTION OF THE VALUE ACCELERATION (PRINCIPAL STATISTICAL CHARACTERISTICS).

Division of the System	Number of Determinations	$\bar{x} \pm m$	σ	Variability Coeff. v	D (Difference)
		a) In Original Condition			
Retina	59	13 ± 0.13	1	7.7%	
External Corpus Geniculatum	198	15 ± 0.15	2.1	14%	
Visual Cortex	209	17 ± 0.15	2.2	13%	
		b) During Accelerations of 1.5 - 5 units.			
External Corpus Geniculatum	43	12 ± 0.15	1.0	8.3%	$D_{a-b}<0.01$
Visual Cortex	43	15 ± 0.15	1.0	6%	$D_{a-b}<0.01$
		c) During Accelerations of 5.1 - 12.0 units			
Retina	108	17 ± 0.29	3.4	8.2%	$D_{a-c}<0.01$
External Corpus Geniculatum	108	18 ± 0.22	2.3	12.8%	$D_{a-c}<0.01$
Visual Cortex	136	23 ± 0.14	1.4	15%	$D_{a-c}<0.01$
		d) During Accelerations of 12.1 - 22.0 units			
External Corpus Geniculatum	62	18 ± 0.16	1.3	7.2%	$D_{c-d}>0.9$
Visual Cortex	55	33 ± 0.78	5.8	17%	$D_{c-d}<0.01$

We can see from the data presented in the table that, during the action of accelerations with values up to 5 units, the latent periods for responses of the external corpus geniculatum, as well as the visual cortex, are somewhat shortened. The variability in the responses is reduced (the coefficient of variability v decreases for the responses of the visual cortex from 13% to 6%, and from 14 to 8.3% for the responses of the external corpus geniculatum). Very different changes are observed during the action of accelerations with values from 5.1 to 12 units. In this case, the latent periods for responses in all the divisions of the optic analyzer increase significantly. We can see from the table that the increase in the latent period of responses for the retina and the visual cortex cause this. The difference between the latent periods of responses for the external corpus geniculatum and the retina even decrease somewhat in this case. /160

The latent periods for the responses of the visual cortex increase even more sharply during the effect of accelerations with values from 12 to 22 units. In those rather few experiments when the responses of the visual cortex remained the same for such values of acceleration, their latent period was increased by a factor of two relative to the original.

Thus, if the intensification of the retardation processes (primarily in the neurons of the retina) is caused by a lengthening of the latent period for the response of the visual cortex during the action of accelerations with average values, then during the action of accelerations with greater values it is caused mainly by a change in the functional condition of the cortical cells themselves.

The ERG and the PR for divisions of the optic analyzer also change significantly during the subsequent period. In relation to the elapsed time since the moment of termination of the acceleration, the nature and significance of the changes vary. Immediately after the action of accelerations with small and average values, the latent period for the responses is somewhat shortened in most cases. This is frequently combined with a significant intensification of the positive as well as the negative phases of the response. These changes indicate that the nerve elements of the cortex and of specific thalamic formations are in a state of increased excitation during this period. However, the phenomena of excitation change rather rapidly with a significant intensification of the retardation process, which is indicated both by a decrease in the amplitude of the responses and by a significant lengthening of their latent periods.

These examinations showed that the transition of the nerve cells to a retarded condition can be temporarily prevented, while the retardation which occurs can be eliminated by a recurrent effect of an acceleration. This fact gives us cause to assume that the origin of the development of these phenomena is not found in the nerve cells for the corresponding division of the analyzer, but is found in the effects deriving from other divisions of the central nervous system. The "reciprocity" in the changes in excitability for the retina and the visual cortex, which is particularly characteristic for the subsequent period, also confirms this assumption.

The recordings in Figure 2 show the phase character of the changes in the electric responses of the retina and the visual cortex.

We can see from Figure 2 that the effect of an acceleration with a value of 13.2 *eg* was accompanied by a significant change in the ERG and the PR of the visual cortex. In the electric responses of the retina, there was a clear decrease in the amplitude of the negative phase, combined with an increase in the positive phase.

The positive component of the response of the visual cortex also decreased substantially. As for the responses of the external corpus geniculatum, their amplitude even increased somewhat during this time.

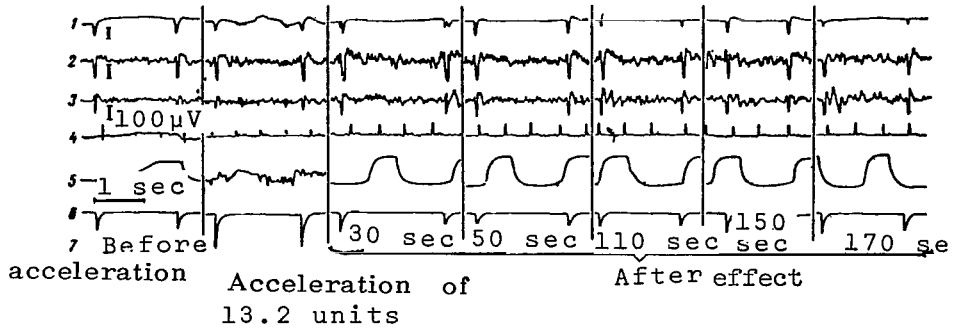

Fig. 2. ERG and PR for External Corpus Geniculatum and Visual Cortex during Acceleration and during the Subsequent Period (1) ERG; (2) Electrographs of the External Corpus Geniculatum; (3) Electrographs of the Visual Cortex; (4) Electrocardiogram; (5) Respiration; (6) Light Flash; (7) Course of Rotation in the Centrifuge. /161

Within 30 sec after an acceleration, the amplitude of the responses on the part of the external corpus geniculatum increased to an even greater degree. The responses of the retina changed even more sharply than during the period of accelerations. The "*B*" wave expanded and seemed to be composed of two waves. The electrical responses of the visual cortex were very much changed. The amplitude of the positive phase for the response became even higher than the original during this time.

Within 50 sec from the moment the accelerations were stopped, the amplitude and the form of the electric responses on the part of the retina and the visual cortex again changed significantly. The amplitude of the responses of the retina became greater than the original. The amplitude of the responses on the part of the visual cortex increased almost by a factor of 1.5, while the negative component increased significantly in this case. During this same period, the amplitude for the responses of the external corpus geniculatum, however, decreased somewhat. Even within 60 sec, there was again a sharp oppression of the responses for the retina, which was combined with a simultaneous increase in the amplitude of the responses for the external corpus geniculatum and the visual cortex. In the responses of the latter, there were additional components. Somewhat later (within 2.5 min after the termination of the accelerations) the amplitude of the responses from the retina again increased significantly, and the amplitude of the responses for the visual cortex decreased substantially in this case. After another 20 sec, these phenomena repeated themselves. Thus, in the changes of the level of excitability for the retina /162 and the visual cortex, there were noted unique, apparently reciprocal

relationships.

The studies showed that even when the responses of the retina are greatly weakened, the responses of the external corpus geniculatum remain slightly changed in a number of cases (Fig. 3). As we can see from Figure 3, an acceleration of 20.3 units caused a sharp depression of the retinal responses. Their amplitude decreased by 3.5 times, while the latent period increased almost by a factor of 1.5. The length of time for the negative phase of the responses changed substantially. While it was about 100 msec before an acceleration, it was only about 25 msec after it. Despite this fact, there were no sharp changes in the electrical response of the external corpus geniculatum. Their latent period and amplitude remained almost the same as before the action of the acceleration. As for the length of time for the positive phase of the responses, on the other hand; it even increased somewhat (from 75 to 90 msec). All this indicates that there appeared to be a transformation mechanism in the action during this period, which guaranteed that the intensity of the excitation would remain constant during a sharp weakening of the afferentation occurring in it.

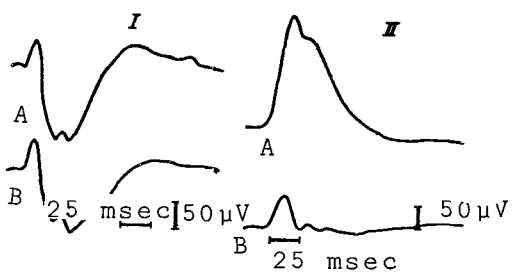

Fig. 3. Responses of External Corpus Geniculatum (I) Against a Background of Sharp Suppression of Responses of the Retina (II) during the Action of an Acceleration of 20.3 units ("Head-Pelvis") (Averaged Data). (A) Before the Acceleration; (B) After It.

As we have shown earlier, the nerve structures of the upper tubercles of the lamina quadrigemina have the greatest stability in relation to the effect of acceleration. Their responses changed less sharply during the subsequent period also (Fig. 4). We can see from Figure 4 that after the effect of accelerations with small values (4.2 units), when the electric responses of the visual cortex and external corpus geniculatum were almost the same as the original ones, the amplitude of the response on the part of the higher tubercles increased substantially. After an acceleration of 12.8 units, when the amplitude of the responses on the part of the visual cortex and external corpus geniculatum proved to be sharply decreased, the amplitude for the responses of the upper tubercles almost did not change, and only the negative phase of the response was intensified. Finally, after recurrent action of accelerations, when the responses of the visual cortex and external corpus geniculatum are not detected the reaction of the nerve structures in the upper tubercles continued to be clearly evident.

As follows from the data being examined above, the effect of /163 an acceleration causes significant shifts in the functional condition of all the divisions of the optic analyzer. The retina and the visual cortex have the greatest reactivity in relation to this effect, and the tubercles of the lamina quadrigemina have the least. The nuclear formations beyond the tubercles occupy an intermediate position.

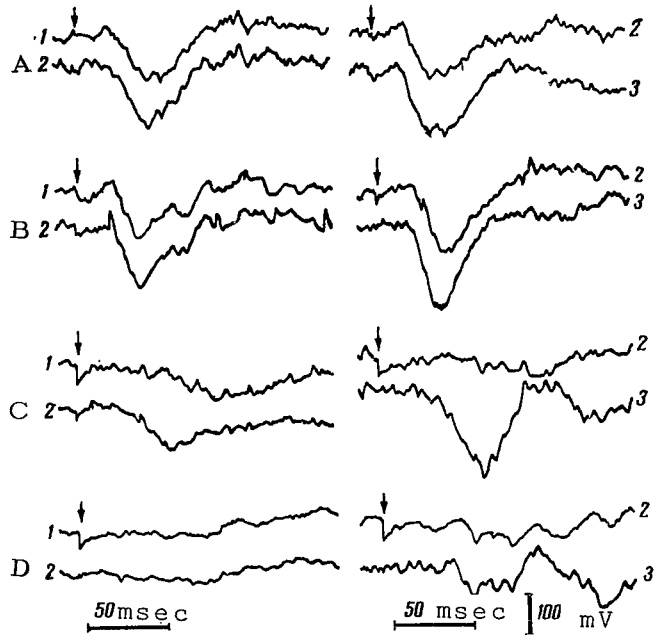

Fig. 4. Primary Responses of the Visual Cortex, External Corpus Geniculatum, and Upper Tubercles of the Lamina Quadrigemina during the Action of Accelerations (Single and in the Form of a Series). (1) Visual Cortex; (2) External Corpus Geniculatum; (3) Upper Tubercles of the Lamina Quadrigemina; (A) Before Action; (B) After an Acceleration of 4.2 units; (C) After an Acceleration of 12.8 units; (D) After a Series of Accelerations (from 8 to 14 units).

The results of these studies show the cortical and retinal nature of the disorders in the activity of the optic analyzer during accelerations. We can assume that these disorders are caused by retardation of the synaptic supply, by a change in the dynamics of the development of the principal nervous processes, and also by a sharp intensification of the background activity for the corresponding nerve centers, which have a concealed effect on the reactions caused by adequate stimulation.

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CHARACTERISTICS OF VEGETATIVE REACTIONS IN MAN DURING THE ACTION OF ANGULAR ACCELERATIONS WITH VARYING VALUES AND DURATIONS

B.I. Polyakov

ABSTRACT: It was established that a single application of negative acceleration from 15° sec^2 (duration of action = 6 sec) to 1200° sec (duration of action = 0.15 sec), vegetative reactions can occur in subjects in the form of a retardation of the pulse and respiration, and an increase in arterial pressure. In most cases, the reactions have a latent period of not more than 20 sec, and they do not depend on the magnitude of the effect. The reactions also do not depend on the degree of the subjects' resistance to motion-sickness, and they have relatively little prognostic value under the given stimulation conditions. The author discusses the necessity of considering the possible effect of the orienting reaction during a quantitative examination of human vestibular-vegetative reactions, and the parameters of the stimuli used.

The design of manned space flights has presented a number of /165
problems concerning the physiology of the vestibular analyzer. In particular, we have seen the necessity for an accurate knowledge of those physical conditions during which the corresponding vestibular reactions occur. Knowledge of these conditions is necessary, primarily, in relation to the possibility of producing artificial gravitation aboard space objects by rotating them and by the resultant inevitable stimulation of the vestibular analyzer. Moreover, a precise knowledge of the value for adequate stimulation is a certain requirement for vestibulo-metric studies, including selection of the astronauts. Thus, the problem of the quantitative relationship between the value for the vestibular stimulation and the nature of the responsive vegetative reactions is of practical and not merely theoretical interest.

Although a similar formulation of the problem is not new [8, 4], the information acquired was limited and disconnected [5-7, 11, 13, etc.]. In a number of cases, a quantitative evaluation of the stimuli was not sufficient, because until recently there was a lack of corresponding methodological possibilities.

The purpose of this study was to characterize the vestibular-vegetative reactions in humans (changes in pulse rate, respiration,

and arterial pressure) during the action of accurately-measured angular accelerations with varying values and length of time for effect.

The studies were conducted on healthy subjects: 19 men and 19 women, ranging from 19 to 36 years of age, who had not had any ear trouble. In all, 85 observations were made. The vestibulometric observation of the subjects was made with the aid of a test-stand (VU-3)[1] in a light-tight chamber. The rotation was regulated on the hour, beginning with an angular acceleration of 3-5°/sec^2, which lasted until the given angular velocity was reached. After a period of uniform rotation lasting 2 min, movement of the seat was stopped. In each experiment, the rotation was produced three times, with varying angular velocities (90, 120, and 180°/sec.). The intervals between two successive rotations were 5-10 min. long.

Four series of observations, with varying parameters for the stimulations, are given in the Table. /166

VALUES OF THE ANGULAR ACCELERATIONS AND TIMES FOR THEIR ACTION

Series Number	Value of the Angular Acceleration, °/sec^2			Time for Action of the Acceleration, sec.	Produce of the Value for Angular Acceleration Within the Time of Its Action		
I	600	800	1200	0.15	90	120	180
II	600	800	1200	0.15	90	120	180
III	45	60	90	2.0	90	120	180
IV	15	20	30	6.0	90	120	180

Series I of the experiments was conducted twice, in order to show the possibility of reproducing the results.

The pulse rate, the rate of respiration, and maximum arterial pressure were measured 10-12 times before rotation, and three times after rotation (with an interval of 20 sec). It was considered that the reaction took place only when the value of the characteristic, during any of the 20-second periods after rotation, differed from the corresponding averaged value before rotation by more than 1.96 σ (R = 0.05).

In each series, we examined 20-22 subjects. Some of the subjects took part in all 4 series of the experiments. The time intervals between the separate series averaged from 8 to 26 days.

[1]Modification of the VU-2 Apparatus [2].

In analyzing the materials, we established that in none of the series for the experiments did the number of subjects for whom the shifts in the vegetative characteristics were found to be reliable, exceed 47.6-50% (Fig. 1). On the whole, changes in the vegetative reactions occurred most frequently in Series I of the experiments, and least frequently in Series IV. The differences in the rate of reactions in Series II and III were insignificant. In all cases, there was a difference in the rate of a change in individual vegetative characteristics during the action of a given stimulus. However, no limitation whatsoever in this relationship was noted anywhere except in Series IV; when the pulse changed most frequently during the action of any stimulus, the respiration changed somewhat less frequently and the arterial pressure changed even more infrequently. In Series I of the experiments, there was a direct relationship between the value for the stimulus imposed and the rate of cases when the respiration changed. During repeated observation (Series II), however, this dependence was not confirmed. At the same time, a direct relationship was found in Series II for the total rate of cases when the arterial pressure changed. remaining series, we did not find any direct relationship between the value for the stimulus and the rate of cases when there were changes in the vegetative reactions.

The reactions occurring in various subjects had various directions. However, in each individual case, once the reaction appeared, it did not change its direction (some /167
single cases). Figure 2 shows the relative number of cases for the appearance of reactions with one or another direction in the various series of the experiments. We can see from the figure that a predominance of cases when the pulse and respiration were slowed

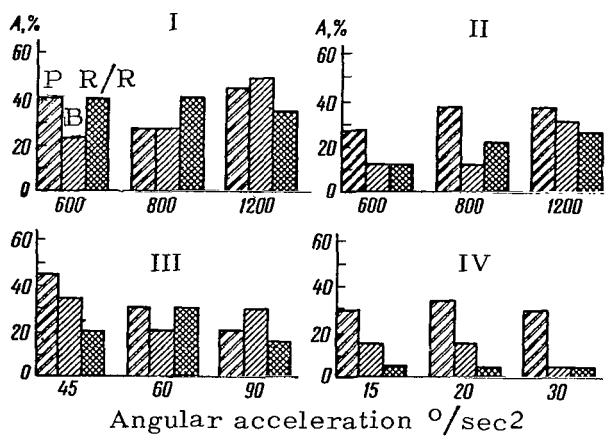

Fig. 1. Rate of Changes in the Subjects' Vegetative Reactions during the Action of Angular Accelerations with Varying Values and Durations (Series I-IV) (as a Percent of the Total Number of Subjects for the Given Series); (*A*) is the Number of Subjects, (*P*) is the Pulse; *B* is the Respiration; (*R/R*) is the Arterial Pressure.

down and the arterial pressure was increased was general for all the series.

It is characteristic that there was no parallelism noted in the changes for the individual vegetative characteristics in the overwhelming majority of cases.

According to the anamnesic data, one group of subjects (45.5%) who took part in Series I and II of the observations had experienced motion-sickness. The remaining subjects had never experienced symptoms of motion-sickness in their entire lives. Therefore, we found it interesting to compare the rate of vegetative reactions in the subjects belonging to another group. In Series I of the experiments, those subjects who had not suffered from motion-sickness showed vegetative reactions which, contrary to all expectations, appeared more frequently than for those subjects who had experienced motion-sickness. However, this difference leveled out during repeated observation. In Series III and IV, the number of subjects who did and did not experience motion-sickness was 4 and 16 (Series III), and 4 and 17 (Series IV), respectively. Therefore, it did not seem possible to obtain a comparative evaluation of the rate of vegetative reactions for the subjects in any group. However, it should be noted that none of the subjects, whether they /168 had or had not experienced motion-sickness, felt any disagreeable sensations in any experiment. The only exception was the subject V-yev, in whom there was noted a moderate nausea lasting about 30 min during the first observation (stimulus of 1200°/sec^2). During repeated observation for 36 days, this subject did not note any disagreeable sensations.

It also seemed general for all the series of the experiments, /169 that the reliable changes in the recorded characteristics were found, in an overwhelming majority of cases, during the first 20 sec after the motion of the seat was stopped. Vegetative reactions began more infrequently within another 20 sec, and even more infrequently within the third 20-second period.

In the experiments, we did not succeed in establishing any reliable differences in the vegetative reactions to stimuli of varying strength. The same was true for the length of time of the reactions: it did not depend on the magnitude of the effect.

The fact that we, as well as a number of other authors [6, 9, 10, 13-17], observed a predominant retardation of the pulse and respiration (parasympathetic reaction) and increase in the arterial pressure (sympathetic reaction) indicates the possibility for simultaneous excitation of both divisions of the vegetative nervous system during vestibular stimulation. However, such a distribution of excitation is not constant and regular.

The brief latent period, observed in most cases, indicates that the reactions observed are of direct vestibular origin, since,

in order to realize the average reactions which can occur during subsequent excitation of the vegetative centers, the reactions of the adrenal glands, the hypophysis, etc., would require a longer period of time [3]. At the same time, we do have reason to assume that the extralabyrinthine effects (intero- and proprioceptive impulses corresponding to a sharp termination of the seat's movement) did not play an important part in the formation of the reactions observed. This is also proven by the fact that there is no reliability in the differences between the magnitude and the length of time of the reactions occurring in Series I of the experiments (sharp termination of the seat's movement) and in Series IV, when the seat's movement was stopped so smoothly that many of the subjects could not even determine precisely when the seat stopped moving completely.

It is of note that the magnitude and the length of time of the vegetative reactions did not depend on the magnitude of the stimulus. This can be explained by the fact that the intensity of the vestibular stimulation was determined, not so much by its absolute value, as by the product of the value for the adequate stimulation during

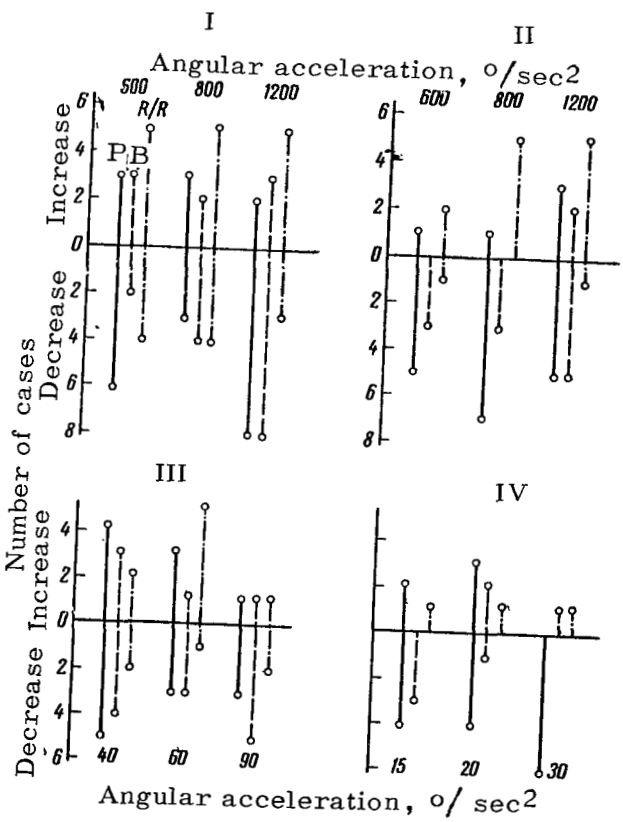

Fig. 2. Direction of the Vegetative Reactions for the Subjects of Series I-IV during the Action of Angular Accelerations with Varying Values and Durations. The Symbols are the Same as in Figure 1.

the time of its action. In relation to the nystagmus reaction, this was also shown by Mulder [12], and (for certain vegetative reactions) by A.V. Lebedinskiy, Yu.G. Grigor'yev, R.M. Lyubimova-Gerasimov, and myself [5]. For such an evaluation, the stimuli in all the series were equal in our experiments.

We should make particular note of the fact that, in a given series of experiments, where only the absolute value for the stimulus changed during the fixed time for its action, there were no reliable differences observed in the intensity of the reactions. We cannot find a sufficiently convincing explanation for this fact. However, it is permissible to assume that the gradient of differentiation in the stimuli for human vegetative reactions during stimulation of the semicircular canals was fairly high, and exceeded that which we selected.

The differences in the results of the various series mainly involve the rate of the reactions. /170 These differences are not really linked to a decrease in the angular acceleration. The difference between the results for Series I and II contradict this idea, because the angular accelerations in both series were identical, and there was no essential difference in the rate of reactions for Series II and III when the angular accelerations varied greatly. These differences in the rate of the reactions can be explained by the assumption that, in the biological sense, the reactions observed were a vegetative component of a general orienting and examining reaction which occurred as a response to every new stimulus. From this point of view, the decrease in the rate of reactions during repeated studies represents suppression of the orienting reaction, while the differences in the intensity of the reactions for different subjects represent the appearance of individual features. Such a concept also explains the negative result obtained by Preber [13] in comparing the vestibulovascular reactions in pilots who showed resistance during training flights and pilots who showed vigorous vegetative reactions in this situation.

Moreover, the observed complex of reactions did not completely correspond to the formal signs of an orienting reaction, and thus had an aspect of specificity. In contrast to the orienting reaction, for which (in addition to an increase in the arterial pressure) an increase in the pulse rate and respiration rate is also characteristic, the reactions of our subjects were characterized by predominant retardation of the pulse and respiration. This also differs from the defensive reaction, which usually occurs at a high energy level, with an increase in the rate of the pulse, an increase in the inspiration tonus of the respiratory center, etc. We can assume that the vegetative reactions we obtained are an integral effect of an interrelationship between the vegetative components of the vestibular and orienting reactions.

The fact of non-conformity (as we have shown) in the character of the vegetative reactions and the anamnesic data give us a basis

for stating that the nature of the change in the pulse rate, the rate of respiration, and the arterial pressure for the subjects during the action of short-period and single-directional accelerations in the range studied, is not related to the vestibular stability of the subject, and can hardly serve as its criterion. This substantiates Preber's opinion [13] that the vascular (and, according to our data, not only the vascular, but also the respiration) reactions under these stimulation conditions do not determine the sensitivity of the subject to rotational tests. However, this does not decrease the significance of these reactions as indicators of the depth of vegetative disorders during the cumulative effect of vestibular stimuli.

We did not succeed in establishing the marginal values of the /171
angular accelerations for the vestibular-vegetative reactions in question. Apparently, in addition to the insufficiently wide range of stimuli, this could be linked with difficulty in separating the specific vestibular-vegetative reactions (i.e., the reactions which have a direct or indirect relationship to the vestibular function) from the general reaction of the organism to angular acceleration, including the vegetative components of the non-specific, orienting reactions. The latter, as we know, are very strong in man. In examining the quantitative relationships between the magnitude of the vestibular stimuli and the subjects' vegetative reactions, we should consider this circumstance: the examinations must be conducted under the conditions of preliminary suppression of the orienting reaction. Moreover, we could use a wider range of stimulation, so that the rate of increase in the stimuli should be fairly steep.

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EFFERENT PULSES FROM THE VAGUS NERVE IN INTACT ANIMALS AND IN ANIMALS WHOSE LABYRINTHS WERE REMOVED, DURING WEIGHTLESSNESS

Ye.M. Yuganov and V.V. Aleshin

ABSTRACT: Efferent impulses from the vagus nerve were studied in intact animals and animals whose labyrinths were removed, under the conditions of short-period weightlessness. It was found that in the intact animals the pulse rate decreases; this effect becomes intensified during the cumulative effect of weightlessness. In rabbits whose labyrinths were removed, the character of the pulses remains practically unchanged. The data obtained show the intermediary mechanisms for the appearance of vestibular disorders, and they can be used for studying the problem of space-sickness.

Having examined the problem on the physiological mechanisms /172
of "space-sickness", some authors link its appearance with a breakdown in the functional operation of the analyzer, as a consequence of the termination of the effect of the force of gravity [3]; others relate it to increased excitability of the receptor formations for the semicircular canals, as a result of a weakening of the retarding effects on the part of the otolith apparatus [1, 7], while a third group links it to the possibility of a specific effect of weightlessness on the otolith apparatus [8].

Naturally, all of the above-mentioned concepts lie within the framework of assumptions, since we are still studying the problem of the character and degree of stimulation for the otolith apparatus during weightlessness and are still attempting to clarify the validity of the physiological theory of the removal of the labyrinths, or the specificity of stimulation of the vestibular analyzer under these conditions. The problem of the particular features concerning the function of the vestibular analyzer during weightlessness could be solved by direct studies of the electric activity of the analyzer at its various levels. Unfortunately, this is still impossible at the present.

In order to study the intermediary mechanisms determining the appearance of vestibular-vegetative reactions, and in order to determine the particular features of the excitability of the vestibular analyzer during weightlessness, we conducted studies (in 1961-1962) of the bioelectric activity of the vagus nerve in intact animals and animals whose labyrinths were removed. We are assuming

that the materials obtained could lead to an understanding of the causes which determine the appearance of disagreeable vestibular-vegetative reactions, and could possibly aid in developing prophylactic measures. Weightlessness was reproduced during parabolic flight of an aircraft, and the duration of the weightlessness was equal to 25-30 sec. In order to solve the problem presented by M.D. Yemel'yanov and V.V. Aleshin, we developed a special method for complete surgical disconnection of peripheral sections of the vestibular apparatus by administering a 1.5% solution of iodoacetic acid to the tympanic cavity. Monoiodoacetic acid belongs to a group of thiocol poisons which react with sulfohydryl groups of the glycolytic enzymatic system, suppress glycolysis, and disturb the process of cellular respiration in this case [2, 4, 5, 6]. Histomorphological examinations of the temporal bones in animals who have had their labyrinths removed by this method showed the 100%- /173
reliability of disconnecting the vestibular apparatus by administering monoiodoacetic acid.

The bioelectric activity of the vagus nerve after distal transverse section was recorded from the central segment of the nerve in the cervical area of animals anesthetized with barbanyl (12 mg/kg). Until now, similar examinations were conducted only under laboratory conditions; we perfected the methodological means which guarantee realization of similar experiments during flight. In particular, we designed a special data unit, which differed from the Tasaki electrodes generally used for such purposes in its lightness, small size, air-tightness, and reliable fixation in animal tissue.

The biological currents of the vagus nerve were recorded with the aid of a loop oscillograph and an on-board electronic physiological device with sensitivity of 100 μV. The potentials were recorded from the entire nerve, and not from its individual fibers. Therefore, during a subsequent analysis of the data, we obtained results only for the rate characteristic of the impulses. We conducted 36 experiments in all.

The results of the studies showed that there are essential changes in the electric activity of an animal's vagus nerve during separate flight seqments. The rate of potentials for the nerve in intact rabbits, during the action of an acceleration with a value up to 2 units, did not change substantially, in comparison with the rate in horizontal flight. Under the conditions of weightlessness, there was a very pronounced suppression of nerve impulses; in a horizontal flight with 70-120 imp/sec, the rate of the potentials during weightlessness usually decreased by 40-70. Figure 1 shows the electric activity of the vagus nerve in horizontal flight, during the action of acceleration and during a period of weightlessness.

The suppression of the electric activity of the vagus nerve during weightlessness reflects the character of the nerve processes

in the vegetative centers, caused primarily by the particular features of the stimulation of all the analyzer systems under these conditions. According to the experiments, we established the fact that in contrast to a single action, a repeated (up to six times) action of weightlessness during one flight causes greater changes in the electric activity of the vagus nerve. These changes occasionally conform to a picture of bioelectric silence (Fig. 1). The effect of suppression of the electric activity of the nerve during the third period of weightlessness is very clearly noticeable in the figure, in comparison with the first. If we assume that the phenomena observed are related to the cumulative action of a stimulus (while weightlessness, just as any other stimulus, has a cumulative property) then it is possible to assume hypothetically that the integration of the nerve processes in the cortical-subcortical formations (occurring in this case) can be the cause for the appearance of the symptoms of "space-sickness". We have not excluded the /174
possibility that, together with other moments, these conditions

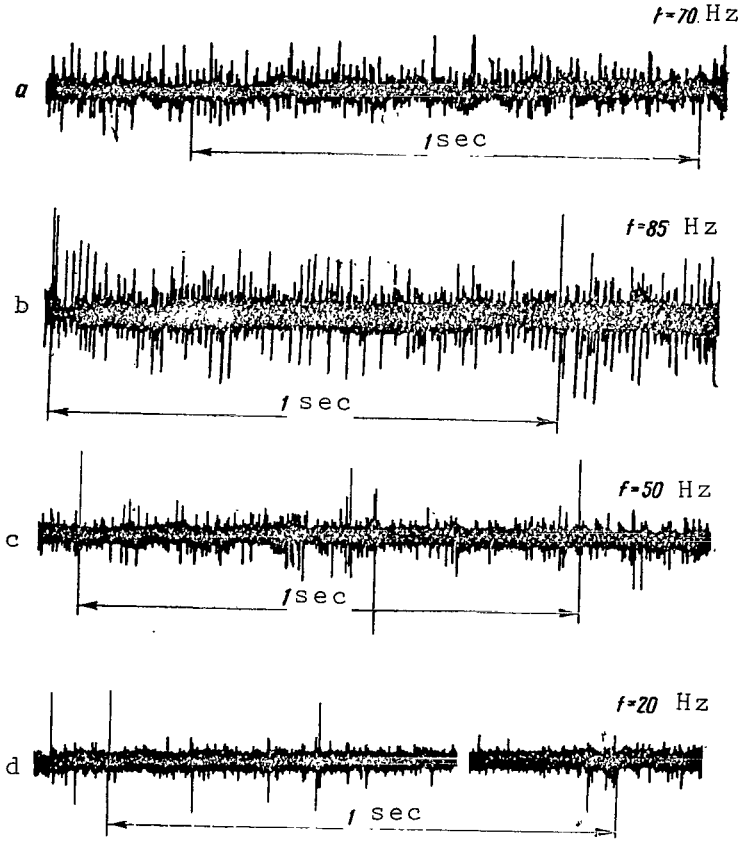

Fig. 1. Bioelectric Activity of the Vagus Nerve for an Intact Rabbit in Horizontal Flight, during the Action of an Acceleration, , and During Cumulative Effect of Weightlessness. (a) Horizontal Flight; (b) Acceleration; (c) Weightlessness, First Vertical Climb; (d) Weightlessness, Second Vertical Climb.

also determine the picture of the vestibular discomfort observed aboard space flights.

In order to determine the individual role and significance of the function of the vestibular analyzer during a change in the electric activity of the vagus nerve as a reaction to weightlessness, we conducted control studies on animals whose labyrinths were removed.

The corresponding experiments showed that the rate of the bioelectric potentials from the vagus nerve in rabbits whose labyrinths were removed did not change substantially under these conditions. During horizontal flight, it was equal to 56-70 imp/sec, and during weightlessness, it was equal to 65-80 (Fig. 2). This allowed us to consider that the suppression of the electric activity for the vagus nerve, during the change in the functions of the complex of analyzer systems during weightlessness, is determined primarily by the stimulation of the vestibular analyzer. The electrophysiological studies conducted allow us to conclude that: /175

(1) A single period of weightlessness lasting 25-30 sec causes (in the intact animals) a decrease in the rate of impulsation for the vagus nerve (cervical section), which becomes intensified

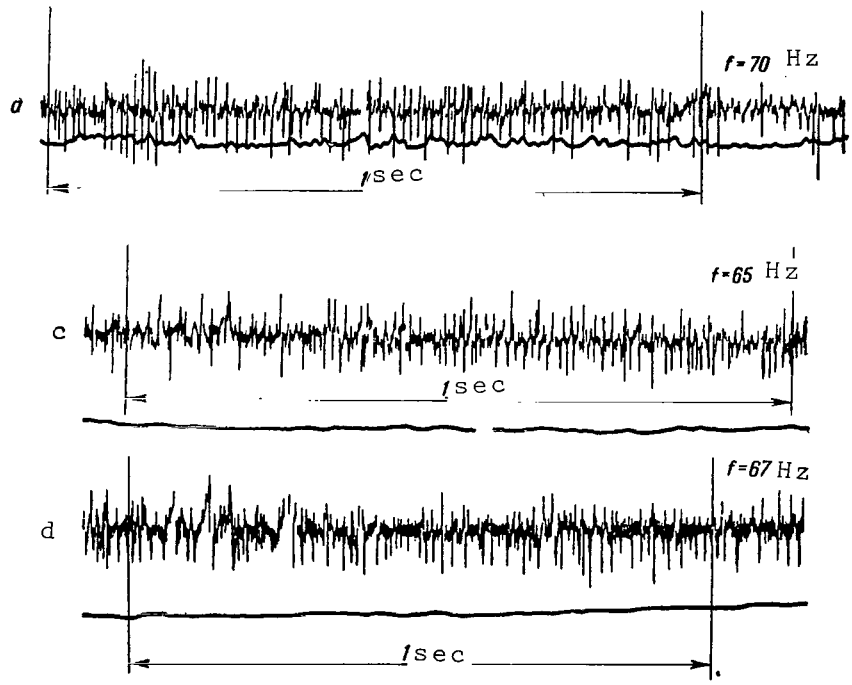

Fig. 2. Bioelectric Activity of the Vagus Nerve in a Rabbit whose Labyrinths were Removed, during Horizontal Flight, and with a Cumulative Effect of Weightlessness. The Symbols are the Same as in Figure 1.

during the cumulative action of this stimulus.

(2) Single and repeated periods of Weightlessness lasting the same length of time practically does not change the character of the bioelectric activity of the vagus nerve in animals whose labyrinths have been removed. The data obtained indicate the particular features of the function of the vestibular analyzer during weightlessness, show the possible intermediary mechanisms in the appearance of vestibular-vegetative disorders under these conditions, and can be used for studying the problem of space-sickness. /176

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THE PROBLEM OF THE INTERRELATIONSHIP BETWEEN THE FUNCTION OF THE SEMICIRCULAR CANALS AND THAT OF THE OTOLITH APPARATUS

S.S. Markaryan

ABSTRACT: The degree of nystagmus was studied in 9 subjects during acceleration in the head region (0.5 and 1.0 units). The data obtained showed that stimulation of the otolith apparatus during the action of accelerations, particularly positive ones, activates the amount of indicators of vestibular nystagmus. During the action of the accelerations, the subjects' sensations of their position relative to the axis of rotation changed.

It is well known that in a number of cases stimulation of the /176
otoliths has a retarding effect on the degree of certain reactions on the part of the semicircular canals.

In experiments with cats, K.L. Khilov [4] established the fact that the duration of nystagmus decreases if the position of the animal's head is changed immediately after rotation. A decrease in the duration of nystagmus was also noted in experiments with human subjects under these conditions [5]. Later, A.P. Popov [3], attempting to show the retarding effect of stimulation of the otolith apparatus with respect to a nystagmic reaction, observed the reactions of human subjects exposed to centrifugal forces. He observed shorter periods of nystagmus in those subjects whose heads /177
were located in the periphery of the centrifuge, in comparison with the case when the subject's head was closer to the center. These data were confirmed later by T.D. Bakhvalova in experiments on cats [1]. She noted that an increase in the centrifugal force is accompanied by shorter periods of nystagmus. Contrasting data were obtained by Ye.M. Yuganov in experiments on human subjects during the action of accelerations in the direction "head-feet" [6]. By these studies, we found that, during the action of accelerations which are constant in value, the length of time for caloric nystagmus increased significantly for all the subjects in comparison with the original value (by 1.5-3 times), while the latent period shortened substantially.

The purpose of this article is to clarify the particular features of the effect of stimulation of the otolith apparatus on the appearance of nystagmic and sensory reactions in man during acceleration in different directions.

In Series I of the tests, we studied the effect of angular and radial accelerations with the subject lying on his back. In

Series II, we studied the effect of the same actions with the subjects on their sides. In Series I and II, we conducted the tests

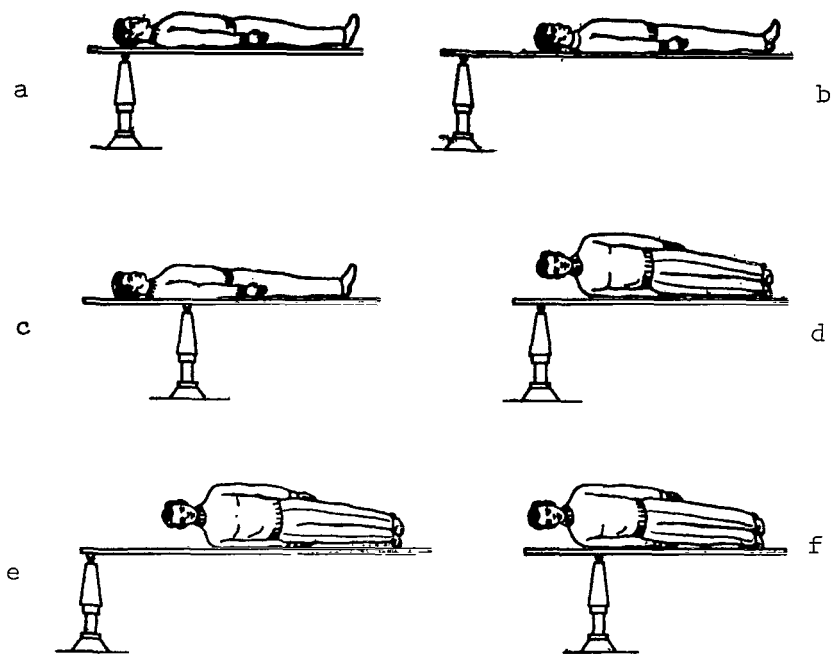

Fig. 1. Schematic Diagram of the Subjects' Position during Rotation.

according to three variations. In the first variation, we took the original position for the subject as the one where the axis of rotation passed through the head region. The acceleration in the region of the head was equal to 0 units in this case. In the second variation, the value of the acceleration was positive, and about 0.5 and 1.0 units in the head region. Finally, in the third variation, the value of the acceleration was negative, also 0.5 and 1.0 units in the region of the head. The velocity of the rotation and deceleration of the seat was fixed for 3 sec. The angular acceleration in this case reached 60 and 90°/sec^2. The velocity of rotation of the seat was equal to 180 and 240°/sec (Fig. 1). /178

Nine healthy men, ranging from 20 to 23 years of age, were subjected to these effects. Ninety tests were conducted.

In each examination, the nystagmus was recorded on an electroencephalograph. The recordings were made by direct observation of the subjects, whose eyes were closed. One pair of electrodes was placed at the outer corners of the eyes, and the other pair was fixed at the upper and lower ends of the orbit so that a line drawn vertically between the upper and lower electrodes would pass through the center of the pupil (the pupils being in a middle position). The curves provided for determining the length of time for the

nystagmus in each case, the total number of nystagmic waves, and their amplitude. The subjects' general condition during the action of the accelerations was determined by their vocal evaluations. The studies were conducted on a universal rotating test-stand [2].

The results of the examinations showed that all the subjects who were lying on their backs or sides (during the action of a positive acceleration) felt heaviness in their legs. The subjects maintained that during the rotation "there was a sensation of falling down, with the feet lowered and the head lifted up". With an increase in the acceleration, these sensations were intensified.

In the tests dealing with the effect of a negative acceleration, the subjects had quite a different impression: it seemed to them that they were rotating with their heads tilted backward and downward. In those cases when the subjects underwent rotation lying on their sides, the illusory sensations of elevation of the head and lowering of the feet, as well as the head moving backward and downward, were somewhat more intense than the sensations felt during rotation when lying on their backs.

The nystagmic reaction appeared in all cases for all subjects, regardless of their position in relation to the axis of rotation, or the direction or magnitude of the acceleration imposed. With an increase in the value of the angular acceleration and the acceleration acting on the head, the nystagmic reaction was intensified.

In the subjects who rotated lying on their sides, there was a significant increase in the nystagmus. In these tests, the nystagmus appeared to be more intense in terms of amplitude, frequency and duration than the nystagmus observed when the subjects rotated lying on their backs. /179

NYSTAGMUS FOR VARIOUS VALUES OF ANGULAR ACCELERATION AND ACCELERATION DEPENDING ON THE SUBJECT'S POSITION IN RELATION TO THE AXIS OF ROTATION (P-ov). (DURATION = 3 SEC).

Subject's Position during Rotation, and Direction of the Acceleration	Value of Angular Acceleration $^\circ/sec^2$	Acceleration in the Head Region, units	Magnitude of Nystagmus
On Back, Axis of Rotation Passing Through the Head Region	60	0	17(63)*
On Back, Axis of Rotation Passing Outside of the Subj. Body, Positive Acceleration in the Direction "Head-Feet"	60	0.5	22(67)

On Back, Axis of Rotation Passing Through the Subj. Body, Negative Acceleration in the Direction "Chest-Head"	60	0.5	17(54)
On Side, Axis of Rotation Passing Through the Head Region	60	0	20(57)
On Side, Axis of Rotation Passing Outside the Subj. Body, Positive Acceleration in the Direction "Head-Feet"	60	0.5	20(63)
Same	90	1.0	41(94)
On Side, Axis of Rotation, Passing Through the Subj. Body, Negative Acceleration in the Direction "Chest-Head".	60	0.5	17(61)
Same	90	1.0	24(83)

*The numbers in front of the parentheses show the duration of the nystagmus (in sec), and the numbers in the parentheses show the number of nystagmic waves in that time.

Let us present the data for the nystagmic reaction of the subject P-ov (Table 1, Fig. 2) as an example of the amount of nystagmus in relation to the angular accelerations and accelerations in the head region, and also in relation to the subject's position relative to the axis of rotation.

As we can see from Figure 2 and the results given in the Table, for a given value of angular acceleration (60°/sec), the intensity of the nystagmus increases in amplitude, rate, and duration during the action of a positive acceleration with a value of 0.5 units. It increases in comparison to the original values for the characteristics of the nystagmic reaction occurring during accelerations (equal to 0 in the head region). During the action of a

negative acceleration of 0.5 units on a subject in the direction "chest-head", there was a tendency for the intensity of the nystagmus to decrease. However, with an increase in the acceleration up to 1 unit, the intensity of the nystagmic reaction increased in amplitude and length of time, particularly during an acceleration in the direction "head-feet" (Fig. 2, VI, VIII). Similar results were also observed for the other subjects. The data presented substantiated the results of Yuganov's observations. /180

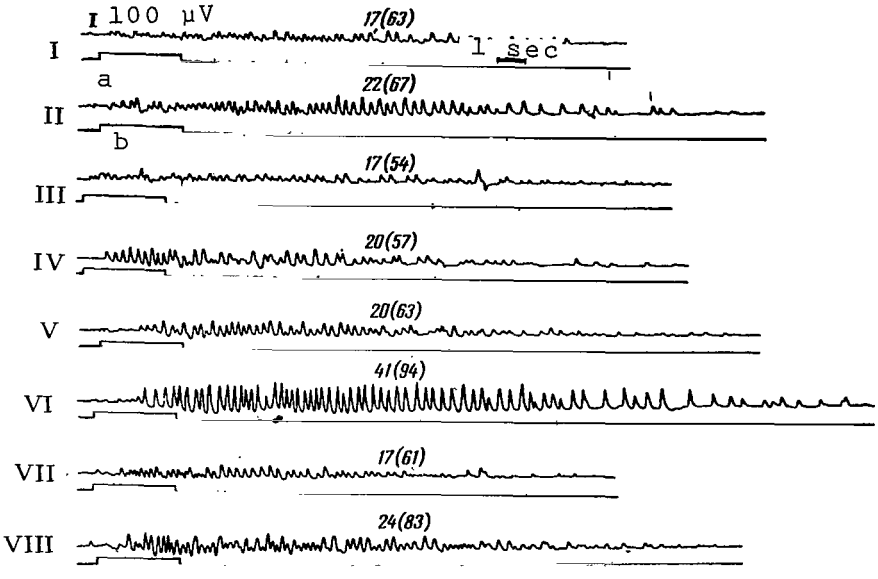

Fig. 2. Nystagmus (P-ov) during the Action of Positive Angular Accelerations of 60 and 90°/sec^2 and Accelerations of 0, 0.5, and 1 units in the Head Region, for 3 min. (a) Nystagmus; (b) Effect of an Acceleration; (I) Position on Back, Acceleration of 0 units; (II) Same, Positive Acceleration of 0.5 units; (III) Same, Negative Acceleration of 0.5 units; (IV) On Side, Acceleration of 0 units; (V) Same, Positive Acceleration of 0.5 units; (VI) Same, Positive Acceleration of 1.5 units; (VII) Same, Negative Acceleration of 0.5 units; (VIII) Negative Acceleration of 1 unit.

The difference between the results of our examinations and the data of K.L. Khilov, A.P. Popov, and T.D. Bakhvalova can be explained by the fact that these authors studied the duration of nystagmus after the effect of centrifugal forces, and not during the period of their direct action.

The subjects' subjective sensations of their position during the action of the accelerations should be considered as the result of stimulation of the proprio- and interoceptors because of a change in the hemodynamics of the organism.

CONCLUSIONS

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(1) Stimulating the otolith apparatus by exposing human subjects to accelerations, particularly positive ones, increases the intensity of the nystagmic reaction.

(2) The effect of acceleration in various directions coincides with the appearance of illusory sensations regarding the body's position in space, which differ for the effects of positive and negative acceleration.

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CUMULATION OF STIMULI IN MOTION SICKNESS

I. D. Pestov

ABSTRACT: During rocking and nonuniform rotation of dogs, their pulse rate and rate of respiration remain relatively constant; there is, however, a constant increase in the excitability of the emetic center, which is found in the emetic reaction to the administration of apomorphine in subcritical doses. The formation of an emesis of any etiology leads to sharp and regular changes in the rate of heart contractions and respiration. The process of the cumulation of stimuli during motion sickness is linked with the function of the emetic center, which transmits (up to a certain limit) the afferent impulses to the centrifugal part of the reflex arc and then, being stimulated intermittently, causes vomiting and the vegetative changes corresponding to it.

At the present time, we know that under the conditions of /181
short-period [11,13] and long period [6] weightlessness, there is a real possibility that a syndrome suggesting motion sickness will develop. This syndrome, known also as seasickness and airsickness, vertigo, etc., has been of great interest to researchers for a long time. Nevertheless, many aspects of its pathogenesis are still not very clear. This naturally limits the possibility of constructing an effective system of prophylactic methods.

A characteristic feature of the dynamics of the development of motion sickness is the fact that nausea and emesis (as well as the accompanying disagreeable subjective sensations and certain vegetative reactions) come in fits and seizures after a period of varying length during which the organism is in a rather satisfactory condition. The reason for this phenomenon, according to the opinion of N.N. Lozanov [5], V.I. Voyachek [3], and S.N. Khechinashvili [9], is the process of cumulation of stimuli. Lozanov assumes that cumulation can be caused either by a summation of the electric potentials of by a build-up of the stimulating material (of chemical /182
nature) in the vestibular centers. It is very probable that such phenomena do make up an integral part of the process for cumulation of stimuli. However, the theory that they are developed at the level of the vestibular centers has not been substantiated by any experimental data. I.I. Bryanov and F.D. Gorbov [2] see the key to understanding the cumulation process in the study of the inductive relationships among the nerve centers. K.L. Khilov [10] considers that the abrupt appearance of somatic and vegetative reactions during motion sickness is the result of a decrease in the

inhibitory function of the cortex. Such generalized concepts do not allow us to draw any direct conclusions regarding the level at which the stimuli cumulate.

In the studies of Bard [12], Wang and Chinn [14], it has been shown that the vestibular section of the cerebellum (nodulus, uvula, pyramis) and the chemoreceptor zone of the emetic center located at the bottom of the IVth ventricle, to the emetic center located in the vicinity of the dorso-lateral margin of the lateral reticular formation of the medulla oblongata. The combination of these central links for the reflex arc causes the periodic appearance of vomiting seizures when the animals are rocked. We can assume that the emetic center is also the focus at which the stimuli accumulate, and that it is periodically discharged, thus leading to a development of generalized seizures of motion sickness. In order to confirm or deny this assumption, we compared the character of the external signs of motion sickness (behavioral reactions, rate of the pulse and respiration) with the dynamics of the change in excitability of the emetic center, in chronic experiments on dogs.

Experimental motion sickness was reproduced on test-stands with nonuniform rotation and vertical and oblique rocking.

RESULTS

Rocking, as a rule, caused latent forms of motion sickness in dogs, while a self-maintained emesis did not develop. The animals' behavior at this stage was characterized by the following features. At the beginning of the nonuniform rotation or rocking, the dogs showed unrest which was expressed in motor excitation and vocal reactions. However, they soon (within 1-2 min) became quiet. After 10 minutes of rotation or rocking, a certain unrest again began to appear, which sometimes changed to a condition of retardation. In this case, the animals periodically licked their jowls, whimpered, /183 and yawned. We considered such reactions to be an expression of discomfort. We did not note any changes in the activity of the cardiovascular and respirational systems, which would correlate with the appearance of the first signs of discomfort. An analysis of the electrocardiographs during the nonuniform rotation or rocking showed the following: in 64% of the cases, within 1-2 min after the effect, against a background of a reaction of general excitation, the rate of heart contractions increased. Subsequently, there did not appear any definite tendencies for the rate of heart contractions to change (even including the time when the first signs of discomfort appeared) (Fig. 1); in 17% of the cases, during the first minutes following the stimulus, there was a decrease in the rate of heart contractions, after which the pulse became stabilized; in 19% of the cases, the rate of heart contractions either did not change within the duration of the entire experiment, or there were insignificant oscillations of the pulse rate, both in the form of an increase and in the form of a decrease.

The directionality of the changes on the part of the respiration was characterized by approximately the same percentage relationships.

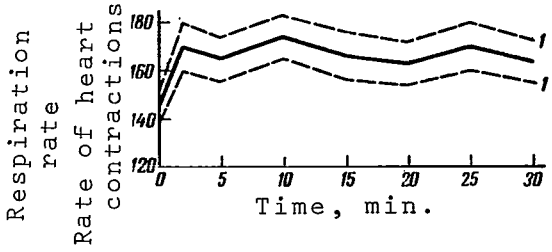

Fig. 1. Average Values for the Rate of Heart Contractions for Dogs during Nonuniform Rotation and Rocking Lasting a Minimum of 30 min. (1-1) Margins for the Average Error in the Characteristics of the Heart Contractions.

At the beginning of the experiment, the animals sometimes showed a pronounced type of motion sickness, with nausea and vomiting. In these cases, the signs of discomfort gradually progressed, the unrest was intensified, the animals began to lick their jowls more frequently, there was an outflow of saliva from the oral cavity, and the respiration became sharply intensified; there were signs of vomiting, and, finally, vomiting. Against the background of the sharp intensification of the respiration, which we considered an indicator of nausea, the rate of heart contractions rapidly increased and reached a maximum immediately before the signs of emesis. During the periods of signals of emesis, and during the emesis, bradycardia developed. This was caused, in our opinion, by an increase in the intrathoracic pressure as a result of energetic contractions of the respirational and thoracic musculature during emesis. Immediately after emesis, tachycardia resumed, but the rate of heart contractions returned to its original level only after several minutes (Figs. 2, 3, and 4).

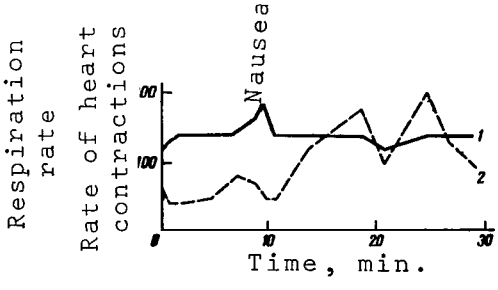

Fig. 2.

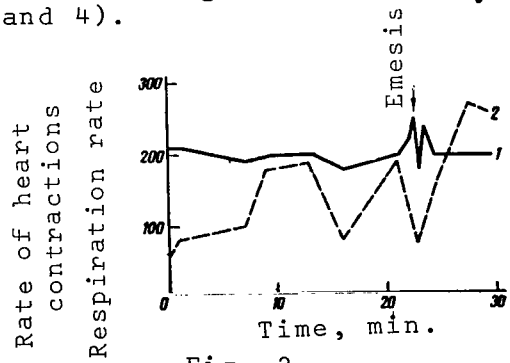

Fig. 3.

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Fig.2. Rate of Heart Contractions and Respiration in the Dog "Kometa" during Vertical Rocking in a Cycle of 52 Rocks/min. (1) Heart Contractions; (2) Respiration.

Fig. 3. Rate of Heart Contractions and Respiration in the Dog "Tuchka", with Oblique Rocking in a Cycle of 40 Rocks/min. Symbols as in Fig. 2.

We can see from the figures that the most significant disorders in the activity of the cardiovascular system are functionally linked with the formation of an emetic reflex. Respiration, as the most labile function, can also change within a wide range before emesis, but these changes do not have a regular character. However, during formation of the emetic reflex, the rate of respiration, as a rule, becomes stabilized for the dogs within a range from 40 to 70 movements per minute, while the intensity of respiration in this case increases sharply.

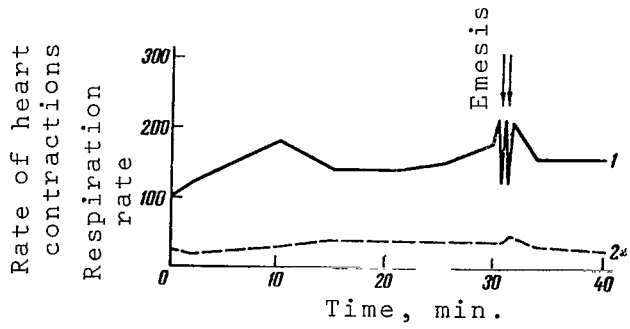

Fig. 4. Rate of Heart Contractions and Respiration in the Dog "Astra" during Nonuniform Rotation in a Cycle of 12 rpm. Symbols as in Figure 2.

There are similar changes in the activity of the cardiovascular system and the respiration under the conditions for formation of emesis, caused by other stimulations [7,8].

The emesis occurring from an intake of apomorphine is accompanied by the same secretory (outflow of saliva), signaling, and motor effects which are also noted during motion sickness. /185 This indicates that the above-mentioned vigorous cardiovascular, respirational, secretory, and motor reactions are related to the functional companions for the emetic reflex which appears during intermittent activation of the effector mechanisms for emesis.

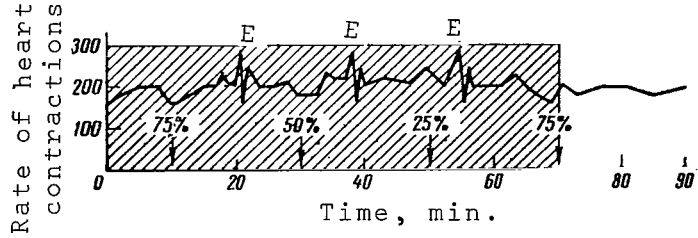

Fig. 5. Effect of Administering Apomorphine in Subcritical Doses in the Dog "Tuchka" during Nonuniform Rotation in a Cycle of 12 rpm. The Arrows show the Moments when Doses of Apomorphine were Administered (as a Percent in Relation to the Value for a Critical Dose during Rest); *E* is the Emesis; the Shaded Part of the Figure shows the Period of Rotation.

By applying subcutaneous injections of apomorphine in subcritical doses, we succeeded in establishing the fact that, during the experiments with nonuniform rotation or rocking, the excitability of the emetic center increases regularly in dogs. Such an increase in the excitability of the emetic center is characteristic even

of the beginning, latent forms of motion sickness, during which, as we have noted, there are no pronounced disorders on the part of the principal vegetative functions. The greater the magnitude of the accelerations acting on the organism, the sooner the subcritical doses of apomorphine are sufficient for causing emesis. Figure 5 shows the rate of heart contractions in the dog "Tuchka" during a regime of nonuniform rotation at 12 rpm, which led to a development of the beginning form of motion sickness in her. During the course of this experiment, the excitability of the emetic center was determined by a subcutaneous administration, repeated four times, of apomorphine in subcritical doses.

As is made clear from the results of this experiment, within 10 minutes of the rotation a dose of apomorphine consisting of 75% of the critical amount seemed effective. Within 30 minutes, a 50% dose of apomorphine caused emesis, and within 50 minutes, a 25% dose also caused emesis. Immediately after rotation was stopped (in the 70th minute of the experiment), a 75% dose of apomorphine proved ineffective. From the control experiments established under conditions of rest, we established the fact that during the 20-minute intervals between successive injections of apomorphine, there is no possibility for integration of the following doses with the preceding ones. Therefore, the results of this experiment, like those of many others, show an increase in the excitability of the emetic center which has a progressive character and is caused by the effect of acceleration. It is significant to note that as the excitability of the emetic center increases, the emetic seizure develops more rapidly after the injection of apomorphine. The number of such emetic seizures does not depend on the level of excitability for the emetic center. This is also confirmed by statistical data. /186

The distribution of emetic seizures in time, from the moment the apomorphine was administered to the eight dogs at rest, and during the beginning stages of development of motion sickness, is given in the table below.

DISTRIBUTION OF EMETIC SEIZURES IN TIME, FROM THE MOMENT WHEN APOMORPHINE IS ADMINISTERED

Dose of Apomorphine	Conditions of the Experiment	Time for the Onset of Emesis After Administering the Apomorphine, min				Number of Seizures
		1-5	6-10	11-15	16-20	
Critical	Rest	9	125	66	30	230
Subcritical	Rotation and Rocking	24	85	31	10	150

The average time for the latent period of emetic seizures

during rest is 10.6 ± 0.25 min, while it is 8.4 ± 0.32 min during increased excitability of the emetic center. Subsequently, in the second case, the critical level of excitability for the emetic center is reached more rapidly, after which there is a "discharge". However, the after effect of such a "discharge", judging from out statistical data, does not depend on the original level of excitability for the emetic center. The relationship between preliminary and repeated emetic seizures in a series is identical for critical and subcritical doses and is in the proportion 4:3.

In our opinion, the data presented indicate that the cause of the appearance of emetic seizures and vegetative disorders which are functionally related to it, during motion sickness, is the process of cumulation of stimuli in the emetic center. This process is intensified during a gradual, sympton-less increase in the excitability of the emetic center, all the way to a definite critical level, after which a vigorous seizure of such disorders is developed. The function of the emetic center thus guarantees dispersion of the afferent impulses arising during acceleration, to the centrifugal part of the reflex arc, which can be considered as the appearance of the organism's compensatory reaction. Because of such a mechanism, the development of vigorous seizures of vegetative disorders during rotation and rocking is frequently impossible. As for the /187
uncomfortable sensations and certain changes on the part of the higher nervous activity, it is well known [1, 4, 5] that they can develop during motion sickness even before the onset of emesis, and they do not always have such a pronounced discrete, intermittent character as was noted for the principal vegetative disorders. Therefore, their functional relationship to the process of cumulation of stimulations in the emetic center still needs to be proven. It is possible that these reactions appear at some critical value for the excitability of the emetic center and gradually increase, reaching a peak at the maximum critical level for excitability of the emetic center. The presence of a relationship between the sensory reactions and the functional condition of the emetic center is indirectly confirmed by the well-known fact that emesis (or, in other words, "discharge" of the emetic center), involves a subjective feeling of relief during motion sickness.

The data presented, in our opinion, reveal certain new possibilities for constructing a system of methods intended for prophylaxis of motion sickness. One such possibility involves an increase in the functional capacity of a natural compensatory mechanism which maintains the dispersion of the afferent impulses occurring during accelerations to the centrifugal part of the reflex arc.

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MATHEMATICAL MODELING OF THE FUNCTION OF THE VESTIBULAR APPARATUS DURING WEIGHTLESSNESS

N. A. Chekhonadskiy

ABSTRACT: The problem of applying methods of mathematical modeling to the study of the function of the otolith section of the vestibular apparatus is examined. The characteristics of the model for the utricular receptors during the action of acceleration on an organism are presented. The presence of certain general rules in these cases, expressed in the appearance of an alternating component at the outlet of the "integrator", is established.

In order to study the vestibular analyzer during weightlessness in more detail, we attempted to make a mathematical model of the functional features of its otolith section. /188

ELEMENTARY MODEL OF THE OTOLITH RECEPTORS

The otolith receptors of mammals, fish, and birds can be divided into the following two types: Type I are the goblet-shaped hair cells; Type II are cylindrical receptor cells [2, 3, 11, 12].

Fish have only Type II cells in the utricle, capped by a bundle of stereocilia supporting a large otolith, and one oriented mobile cilium.

For mammals, in addition to the cylindrical hair cells (Type II), there are also cells of Type I, which are particularly developed in birds [3].

The Type I cells are also capped with a bundle of stereocilia, which support the otolith membrane with minute otoliths, and with one oriented mobile cilium in each cell.

Thus, in examining the cellular and subcellular organization of the hair cells in vertebrates, we can determine certain general features which are characteristic for cells of both types; these are the otoliths, the bundle of stereocilia, and the one mobile cilium located single in all the cells.

In the opinion of Ya. A. Vinnikov [3], this indicates the immutable character of stimulation and the uniqueness of receiving the stimulus in the utricle of vertebrates, regardless of the environment and despite the simultaneous sharp evolutionary reorganization of that part of the cell where the excitation is transmitted

to the corresponding cynapse.

However, the nature of stimulation of the otolith receptors is still not clear. In our studies, we did not go into an examination of the actual nature of stimulation of the "organ of gravitation" for vertebrates, but attempted to present a very simple model of the otolith receptor, which would describe to some degree the function of receptors of both Type I and Type II.

The latter condition has exceptionally important significance in modeling the function of the vestibular apparatus during weightlessness.

In designing the model, we considered that the otolith receptor converts the force acting on the otolith to electric pulses whose rate is proportional to this force. /189

The receptor reacts to a movement of an animal's head relative to the vertical as a result of a change in the value of the component forces for the weight of the otoliths, directed along and across the hairs which are linked in some way with the otoliths. The converters of the values for these forces into the rate of the pulses are sensitive cells located at the base of the stereocilia.

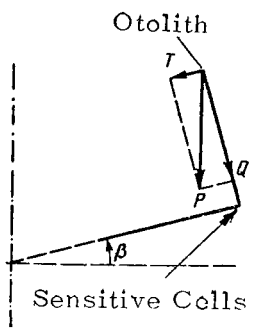

Fig. 1. Schematic Diagram of the Model of the Otolith Receptor. P is the Force of the Weight of the Otolith; Q is the Component of the Weight Force, Directed Along a Hair; T is the Component of the Weight Force Directed Across a Hair; β is the Angle of Lift for the Utricle Relative to the Horizontal.

A schematic diagram of the receptor model is given in Figure 1.

Thus, one of the principal concepts of the model we developed is the idea that information regarding the value of the forces acting on an organism is determined by the rate of the receptor impulses, which subsequently will undergo some conversions in the central section of the vestibular apparatus.

The rate of the receptor impulses, derived from the properties of the model and in the case of its linear dependence on the force received by the receptor, can be represented for the force acting along the hairs in the following way:

$$f = f_0 + \mathrm{k} P \cos(\alpha + \beta), \qquad (1)$$

where f_0 is the background rate of the receptor pulses;

k is the constant of the coefficient of sensitivity;

P is that part of the force of the otolith weight perceived by a given receptor;

α is the angle of inclination for the body relative to the horizontal (in the frontal plane);

β is the angle of lift for the utricle relative to the horizontal.

The coefficient of sensitivity in a general case can also be negative, as a result of which the output value will have the following form:

$$f = f_0 - \mathrm{k}P\cos(\alpha + \beta). \qquad (2)$$ /190

In the case when the receptor reacts only to that force which is directed across the hairs, the rate of its pulses can be determined with the aid of the following relationships:

$$f = f_0 + \mathrm{k}P\sin(\alpha + \beta), \qquad (3)$$

$$f = f_0 - \mathrm{k}P\sin(\alpha + \beta). \qquad (4)$$

Thus, on the basis of the properties of the receptor model we are examining, we can expect that the otolith receptors, depending on the character of their reaction during inclinations from side to side, can be divided into four types.

Type I. The rate of the receptor pulses is maximum in a vertical position. An inclination to either side causes a decrease in the rate of the pulses (Fig. 2 A,I).

Type II. The rate of the receptor pulses is minimum in the vertical position. An inclination to either side leads to an increase in the rate of the pulses (Fig. 2A, II).

Type III. The rate of the pulses decreases during inclition toward the lead, and increases during inclination in the opposite direction (Fig. 2B,IV).

Type IV. The
nation toward the lead, and increases during inclination in the opposite direction (Fig. 2B, IV).

These data coincide with the results of Schone's study on fish, which established the fact that an overwhelming majority of neurons in the vestibular nuclei react in a way similar to the receptors of Type II, and part of them react in a way similar to Type IV. Comparatively few neurons reacted in a way similar to Type II, and no neurons were observed whose impulse activity would be characteristic of Type I [13].

Therefore, we can draw the conclusion that the receptors of the otolith apparatus react primarily to the force directed across the hairs (receptors of Types III and IV). /191

So far, we have been studying the receptor model as a certain converter of the angle of inclination of an animal's head relative to the vertical, in either direction. Let us examine what type of model we can have for the receptor reaction during the action of a constant acceleration.

Let us turn to the principal characteristics of the receptor described in Equations (1) to (4), from which it follows that, for a constant direction of the action of acceleration, the rate of the pulses can be described by the following two types of equations:

Receptor of Type A

$$f = f_0 + k^* G, \tag{5}$$

Receptor of Type B

$$f = f_0 - k^* G, \tag{6}$$

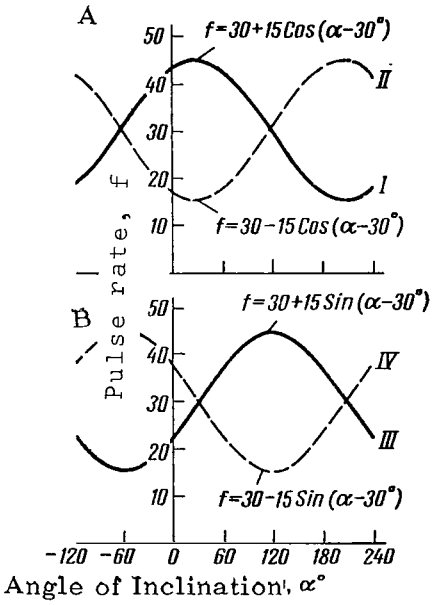

Fig. 2. Rate of Receptor Pulses Reacting to the Force Directed (A) Along and (B) Across the Hairs, in Relation to the Angle of Inclination. Right Utricle. I, II, III, and IV are the Types of Receptors.

where G is the constant acceleration acting on the receptor, and k^* is the coefficient of the receptor's sensitivity to acceleration.

However, the linear relationship between the rate of the impulses and the value for the acceleration acting on an organism, described by Equations (5) and (6), is probably preserved only within a definite range for the acceleration. On reaching a certain value, the dependence becomes non-linear (Fig. 3). Moreover, the non-linearity begins to appear earlier in those receptors which have greater sensitivity, since the coefficients of the receptors' sensitivity enjoy the following relationship:

$$k_1^* > k_2^* > k_3^* > k_4^*. \quad (7)$$

There are also similar relationships for the characteristics shown in Figure 3B, if we examine the following absolute values of the coefficients of sensitivity:

$$|k_1^*| > |k_2^*| > |k_3^*| > |k_4^*|. \quad (8)$$

The presence of a non-linear segment in the characteristics of the receptors, occurring in the case of an effect of a significant acceleration, leads to a substantial change in the characteristic of the receptor after the action of this acceleration is terminated.

Figure 3C shows the characteristic for the model of Type A during an increase in an acceleration to a certain value G_m, when this characteristic has a non-linear segment. This figure also shows the characteristic of the same model during a decrease in the value for the accelerations, from the value G_m to $G = 1$.

We can see from Figure 3C that the rate of pulses for a receptor which has been subjected to the effect of an acceleration will greatly exceed the rate of the pulses corresponding to the value for the acceleration acting at a given moment on the receptor. This probably could also occur during weightlessness, following the preliminary effect of significant accelerations. /192

Therefore, during the first moment of the onset of weightlessness after the spacecraft has entered orbit, we can expect an increase in the excitability of the receptors in the vestibular apparatus.

Earlier, we examined the changes in the rate of receptor pulses in relation to the angle of inclination of the animal's head, and in relation to the value for the acceleration under the condition that the coefficient of sensitivity is either constant or variable, but strictly linked with the value for the angle or the force acting on the receptor.

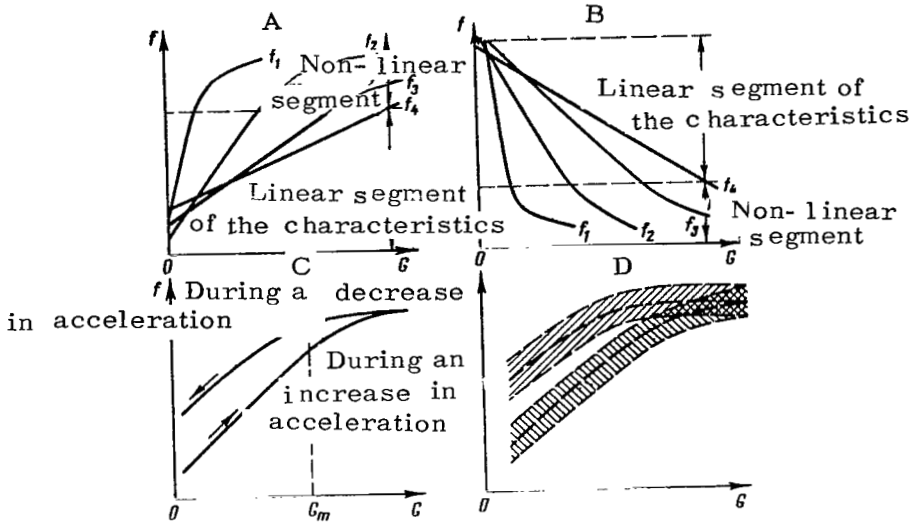

Fig. 3. Characteristics of the Model of an Otolith Receptor during Acceleration.

Actually, such a strict relationship will probably not be found as a result of the variability inherent in biological phenomena.

As a result of the variability in the coefficients of sensitivity, the rate of the pulses during repeated action of a given force can vary.

Figure 5D shows the approximate relationships for the functions we are studying, when the variability of the coefficients is ±15%

of the average value, which is very characteristic for a number of biological phenomena. /193

Therefore, the rate of receptor pulses in relation to the value of the acting acceleration is a random function of this parameter, i.e., it can achieve relatively average magnitudes of any value within the range from +15 to -15%.

Such a feature of the characteristics for the receptors is probably also preserved under the conditions of weightlessness, which determines to a large degree (in our opinion) the features for the functioning of the vestibular apparatus in this case.

CHAIN STRUCTURE OF THE OTOLITH SECTION IN THE VESTIBULAR APPARATUS

In developing a mathematical model of the vestibular apparatus, we must attempt to trace the paths for the transmission of this information in the higher divisions of the central nervous system, giving a mathematical expression for the processes of recoding which can take place.

The electric pulses from the receptor (the vestibular nerve) along the corresponding nerve paths, appear at first "at the input" of one of the neurons at the Scarpa ganglion, and then "at the input" of the neuron of a vestibular nucleus.

The utricle and the saccule contain the greatest numbers of receptors, each of which is linked in series with the neuron of the Scarpa ganglion and the vestibular nucleus.

Therefore, the otolith section of the vestibular apparatus has a chain structure.

There are no cross-relationships between the receptors and the neurons of the Scarpa ganglion, according to contemporary concepts of the structure of this organ. This indicates that in future studies of this problem we can examine the vestibular apparatus from the receptors to the neurons of the vestibular nuclei as a large series of receptor-neuron chains, differing from one another in definite characteristics.

As for such nerve structures as the reticular formation, various interrelationships among the neurons probably play a significant part, which should be considered in studying the principles of encoding the information contained in this nerve formation.

THE VESTIBULAR APPARATUS - AN AUTOMATIC MEASURING AND CALCULATING DEVICE

We can now consider the indications that the receptors of the atrium are stimulated during a change in the position of the body

in the gravitational field, and also during radial accelerations.

In this case, we find the finite function of the utricle and /194
the saccule linked with the continuous established reflexes for the muscles of the extremeties, the trunk, and the neck, and with the so-called symmetrical and asymmetrical vestibular reflexes [3].

Such are the principal functions of the otolith apparatus in higher animals, from the point of view of physiology. From the point of view of cybernetics, the principal function of the vestibular apparatus is the continuous measurement of a number of mechanical values characterizing the position and movement of the organism in space. This process is probably carried out by the receptor formations--the otolith section and the semicircular canals.

In the central section of the vestibular apparatus, there occur the processes of developing the information coming from the receptor formations. The essence of the latter is found in the determination of certain mechanical values which characterize the position and the movement of the organism in space, but which are not measured directly by the otolith receptors [6]. On the basis of these data, the corresponding regulating signals, which guarantee the necessary changes in the animal's position relative to its location and the forces acting on it, are formulated in the central division of the vestibular apparatus.

Therefore, the vestibular apparatus is a certain device which provides for continuous measurement of the values characterizing the position and the movement of the organism in space, and guaranteeing automatic regulation of the motor organs, in order to preserve equilibrium.

COMPARISON OF THE PULSE RATE FOR THE RIGHT - HAND AND THE LEFT-HAND APPARATUS--THE BASIC PRINCIPLE OF THEIR PAIRED OPERATION

Even at the time of Högyes, it was well known that the vestibular apparatus operates as a double organ [12]. Having studied the vestibular reflexes in the eye muscles of rabbits, Högyes drew the conclusion that each eye is affected by both labyrinths, while there is constant excitation from the labyrinths to the eye muscles, not only when the animal is in motion, but also when it is at rest.

Independently of Högyes, and in a more concrete form, the concept of the continuous activation of the receptors of the semicircular canals was formulated by V.M. Bekhterev [1], who showed that the motor reactions caused by intersection of the VIIIth nerve can completely suppress intersection of the opposite nerve.

Therefore, in studying the functions of the vestibular apparatus, many authors have maintained that there were relationships

between the right-hand and the left-hand apparatus. However, these studies did not answer the question regarding the character of these relationships and the quantitative rules which apply in this case. /195

We drew the hypothesis that the basic principle of the paired operation of the vestibular apparatus is the comparison of the rates coming from the receptor formations of the right-hand and left-hand apparatus, accomplished by a certain "integrator" [6-8]. In this case, we are not assuming that there is a special nerve structure which acts as the "integrator". It is possible that the comparison of the pulse rates and the isolation of a varying rate is accomplished by such accumulations of neurons as the vestibular nuclei or the reticular formation.

The hypothesis we presented was confirmed by the experimental study of G.I. Gorgiladze [5,9].

The latter, having studied the mechanisms for the paired operation of the vestibular apparatus in animals by stimulating the labyrinths with direct current, drew the conclusion that there are inhibiting neurons between the right-hand and the left-hand vestibular nuclei.

The presence of an "integrator" can explain the functions and the principles of the action of the mechanisms which regulate the flight organis of birds to fly, as well as the character of the movement of animals and birds with partially-removed otolith apparatus.

REACTION OF THE MODEL DURING THE EFFECT OF ROCKING AND WEIGHTLESSNESS ON THE ORGANISM

Very interesting relationships can be obtained in examining the function of the model during the effect of mechanical oscillations of low rate (rocking) and weightlessness on the organism.

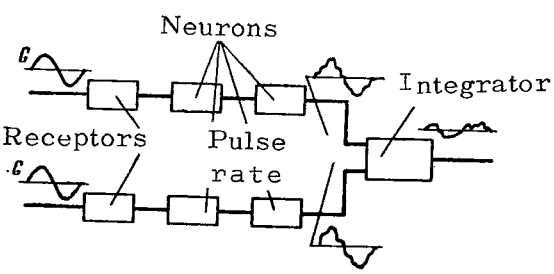

Fig. 4. Schematic Diagram of the Model of the Vestibular Apparatus during Rocking.

Actually, the output value of the "integrator" can take the following form (Fig. 4):

$$F(t)=\int_0^t h_1(t-\tau)G_1(\tau)\,d\tau-\int_0^t h_2(t-\tau)G_2(\tau)\,d\tau, \qquad (9)$$

where $h_1(t)$ and $h_2(t)$ are the pulse transitional functions of the chain of receptor neurons for the right-hand and left-hand utricles; $G_1(t)$ and $G_2(t)$ are functions of the action of an acceleration on the right-hand and left-hand utricles. /196

During the action on an organism of mechanical vibrations with low rate (rocking), when the value for the acceleration acting on the right-hand and left-hand utricles is identical, the output value of the "integrator" will take the following form:

$$F(t) = \int_0^t G \sin \omega\tau \, [h_1(t-\tau) - h_2(t-\tau)] \, d\tau, \qquad (10)$$

where ω is the rate of the mechanical vibrations acting on the organism.

We can show, by solving (10), that during a long period of rocking, when all the aperiodic components are eliminated, the output value for the "integrator" is determined in this way:

$$F(t) = \lambda G \sin(\omega t + \varphi) \qquad (11)$$

where ϕ is the phase shift between the acting force and the pulse rate at the "integrator" output.

The cause for the appearance of the component at the "integrator" output during rocking is the presence of a difference in the characteristics of the receptor-neuron chains in the left-hand and the right-hand utricles. The more the characteristics for the chains of receptors-neurons in the right and left utricles differ, the greater the coefficient λ in Equation (11) and therefore the greater the output value for the "integrator". For an ideal agreement between these characteristics, the output value for the "integrator" during the rocking would always have to be equal to zero.

When the organism is in a state of weightlessness, the receptors in the otolith section of the vestibular apparatus will perceive random displacements of the membrane, because of a lack of equilibrium in the neutral condition (Fig. 5). The latter circumstance causes the value for the pressure of the membranes on the hairs of the receptors in the right and left utricles to vary, while the change will be random in time.

This means that even when the characteristics for the chains of the left and right utricles are identical, the output value for the "integrator" will not be equal to zero, as could happen during rocking.

When a random signal appears at the input for the linear dynamic system, the output value of the latter can be represented only with the aid of the statistical characteristics. It is well

known that the latter most frequently determine the mathematical expectation and the corrlation function [4, 10]. /197

In our case, the mathematical estimate of the output value for the integrator $M_F(t)$ is determined by the following relationship:

$$M_F(t)=\int_0^t h(t-\tau)\,[M_1(\tau)-M_2(\tau)]\,d\tau, \tag{12}$$

where $M_1(t)$ and $M_2(t)$ are the mathematical estimate for the degree of pressure in the membrane on the hairs of the receptors of the right and left utricles.

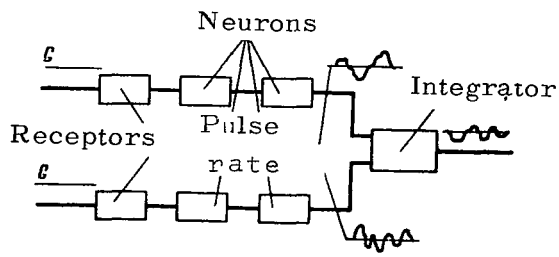

Fig. 5. Schematic Diagram of the Model of the Vestibular Apparatus during Weightlessness.

For the correlation function, the following expression will be valid:

$$K_F(t,t')=\int_0^t\int_0^{t'} h(t-\tau)h(t'-\tau')\,[K_1(\tau,\tau')-K_2(\tau,\tau')]\,d\tau\,d\tau', \tag{13}$$

where $K_1(t,t')$ and $K_2(t,t')$ are the correlation functions for the relationship in time of the pressure at the hairs of the receptors in the membranes of the right and left utricles.

In order for the output value for the "integrator" to be equal to zero while the organism is in weightlessness, it is necessary [as follows from (12) and (13)], the the following conditions be fulfilled:

$$\left.\begin{aligned} M_1(t)-M_2(t)&=0,\\ K_1(t,t')-K_2(t,t')&=0.\end{aligned}\right\} \tag{14}$$

We can easily see that we can have these relationships only in the case when the changes in the pressure of the membranes on the hairs of the receptors in the right and left utricles are produced simultaneously and according to similar rules. Since such a phenomenon is impossible during weightlessness, this will obviously lead to the appearance of a certain component at the "integrator" output.

Therefore, during the action on an organism of periodic vibrations at the output of the "integrator", there is a component which arises as a result of the lack of identity between the characteristics of the receptor-neuron chains in the right and left utricles. In the case of weightlessness, such a component appears even when these characteristics are absolutely identical. The difference between the latter probably increases this "component". /198

Subsequently, the processes which occur in the proposed elementary model of the vestibular apparatus during the action of rocking and weightlessness produce roughly the same effect, i.e., the appearance of a component at the "integrator" output.

From an analysis of the properties of the model, it follows that a good tolerance for a given individual to rocking, explained by an agreement between the characteristics for the right and left "channels", can never indicate a good tolerance to weightlessness.

These are the conclusions of an analysis of the properties in the model being examined. Further studies in examining and perfecting the model itself may possibly aid not only in explaining the individual functions of the vestibular apparatus, but perhaps also in finding ways for regulating these functions.

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APPLYING CORRELATION ANALYSIS TO A STUDY OF THE REACTION OF SINGLE NERVE ELEMENTS IN THE CEREBRUM OF CATS TO STIMULATION OF THE VESTIBULAR APPARATUS BY ROCKING

M.G. Kutateladze, N.V. Merabishvili, and M.D. Venttsel'

ABSTRACT: The reactions of single nerve cells in the visual region of the cerebral cortex (17-18th region according to Broadman) and of the reticular formation of the medulla oblongata (n. gigantocellularis) were examined in cats during rocking. The microelectrode technique was used for recording the potentials of the effect. The results of analyzing the change in the frequency of response showed that a change in the pulse rate is observed in both regions during rocking. In examining the rate for the same neurons, with the aid of the correlation analysis, it was found that the reaction to the magnitude of the rocking is observed in the reticular formation of the medulla oblongata, and is not observed in the visual region of the cortex.

The practice of astronautics has stimulated an interest in /199
the function of the vestibular analyzer under specific flight conditions, particularly during the action of changes in the gravitational field on the organism.

It is well known, in particular, that during flight certain astronauts had illusions regarding their position in space, and showed changes in motion coordination and certain vegetative changes.

During the formation of these reactions, the functional interrelationships between the vestibular analyzer and various divisions of the central nervous system obviously play an important role. The experimental neurophysiological data on this are limited. The purpose of this article is to analyze the reaction of single nerve elements in the visual region of the cerebral cortex (17-18th region according to Broadman) and in the reticular formation of the medulla oblongata (n. gigantocellularis) in cats during adequate stimulation of the otolith apparatus by rocking.

METHODS

The experiments were conducted on anesthetized cats weighing 2.5-4 kg. In the experiments with the reticular formation of the medulla oblongata, we used a chloralose-nembutal anesthesia (40 mg/kg of chloralose and 15 mg/kg of nembutal, given intraperitoneally),

while in the experiments with the cortex we used curarization (diplacin, 5 mg/kg; the animal was given artificial respiration).

The commisural activity of individual nerve elements was recorded extracellularly, with the aid of glass microelectrodes; the external diameter of the tip was 1-2μ. The microelectrodes were filled with a 3 molar solution of KCl.

The microelectrodes were inserted with the aid of a stereotaxic device. The location of the microelectrodes in the reticular formation was determined after fixation of the brain in formalin and staining of celloidin sections.

The respirational and cardiovascular pulsations of the brain were decreased during the experiment by draining the cisterna magne, pneumothorax, and addition of agar-agar (37°).

The animals, together with the stereotaxic device, were placed /200 in a dark shielded cage on an experimental stand, which allowed stimulation of the otolith apparatus. (Vertical dislocation with a linear acceleration of 0.1-2 g).

The pulses from a single neuron were recorded with the aid of a dual-beam oscilloscope.

The preliminary processing of the signals was made by calculating the number of pulses per second and by averaging the data obtained before rocking, during rocking, and after rocking. The reaction of the neuron to the rocking was determined according to the change in the average pulse rate during these three periods. Such a method of calculation proved to be very approximate, and it did not always guarantee determination of the degree of the neuron's reaction to rocking.

In order to obtain a more precise evaluation, we used the method of correlation analysis, which provided for isolating the periodicity of the signals against the noise background. In our case, the periodic signal was the rocking. (The change of the value for the acceleration was sinusoidal).

For a reference formula, we used the following:

$$R_x(\tau) = \frac{\varepsilon_{i=1}^{n-\tau}(x_i - M_x)^2}{D_x(n-\tau)},$$

where $R_x(\tau)$ is the value for the normalized correlation function: X_i is the value for the intercommisural interval; M_x is the average value for the intercommisural interval, $M_x = \varepsilon xi/n$; D_x is the dispersion for distribution of the intercommisural intervals,

$$D_x = \frac{\varepsilon(x_i - M)^2}{n-1},$$

n is the total number of intervals being studied; and τ is the sequence number for the interval, $\tau = 0,1,2,3,\ldots n$.

The determination of the change in the intercommisural intervals is a complicated and difficult operation. In order to introduce the values for the intercommisural intervals into the computer, we used an apparatus for semi-automatic read-out of the information, which provided for transferring the value for the intercommisural intervals directly onto punched tape, on a definite scale, while the image on the photographic film, with the impulse of the neuron recorded on it, was enlarged. Calculation of the correlation functions was made on a "Dnepr-1" computer. The results of the calculations were transferred to graphs, and then fed into the computer again, which determined the period of time and the amplitude of the periodic components with the aid of the method of least squares. For the original curve, we selected the following;

$$R(\tau) = Al^{-\alpha\tau} + B\cos(\omega\tau - \varphi),$$

where the unknown parameters are A, α, ω, B, and ϕ. After the calculations, the machine printed the value for these parameters, and also the value for the points on the approximating curve. The latter were transferred to graphs of the correlation function. Since the correlation function obtained is not a function of time, but a function of the number of the intercommisural interval, the time value for the period of oscillations of the correlation function was determined according to the following formula: /201

$$T \cong \frac{1}{n_1} \cdot M_x \cdot n_2,$$

where n_1 is the number of points obtained from the semi-automatic system for the information output at an interval of 1 sec; n_2 is the number of points fitted into one period of the correlation function.

The results of the calculations according to this method are given below.

We should note that the method applied for processing the data produced good results during stimulation of the animal by any periodic signal (light, sound, etc.), particularly in those cases when the reaction of the neuron to a single stimulation cannot be detected by generally-accepted methods.

RESULTS

We recorded the electric activity from 80 neurons in the visual region of the cerebral cortex. The pulse rate while at rest varied from 8 to 22 pulses per second. During rocking, 52 neurons (65%) increased their activity, while 28 neurons (35%) decreased their activity.

We recorded the impulses from 110 neurons in the reticular formation of the medulla oblongata. 19 of these neurons (17.2%) did not have spontaneous activity: they were activated during the rocking. 91 neurons (82.8%) had spontaneous activity at a rate from 0.4 to 51 per second.

The neurons of the reticular formation in the medulla oblongata were divided into the following three groups, according to the character of their reaction to the rocking: 47 neurons (51.6%) responded by an increase in the frequency of the rhythm; 39 neurons (42.8%) responded by a decrease in the frequency of the rhythm; 5 neurons did not change their rhythm.

The data presented, obtained by statistical calculations, permit evaluating the general differences in the character of the reaction of the neurons in the regions being examined to the rocking. At the same time, the use of correlation analysis provided for tracing the reactions of the neurons during a change in the value of the acceleration during vertical displacement of the animal. The use of this method gave the following results.

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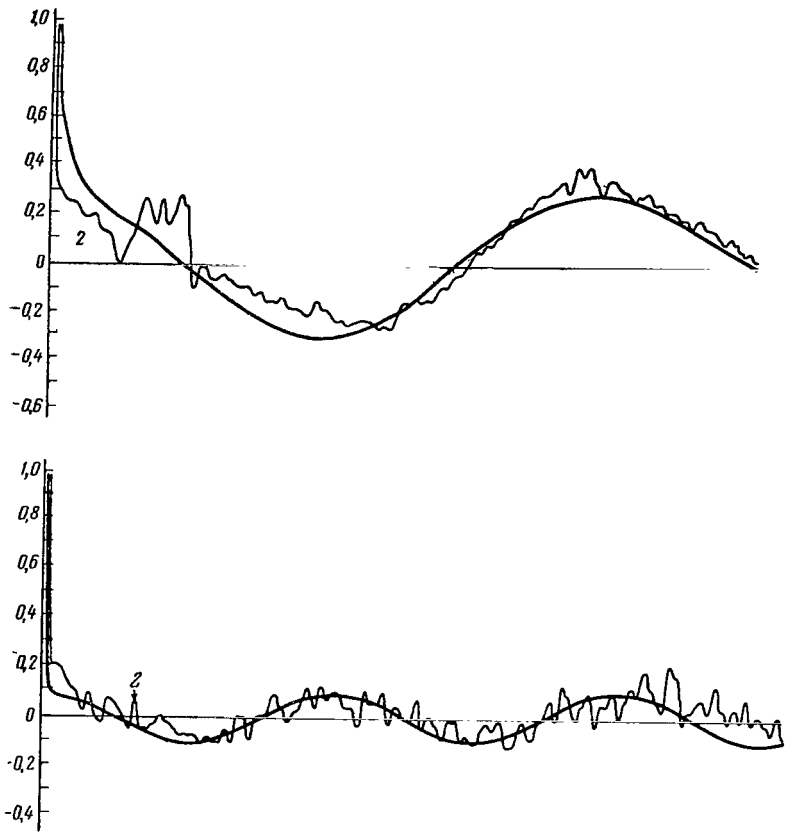

Fig. 1. Actual (2) and Approximate (1) Correlation Functions of the Intercommisural Intervals for a Neuron in the Reticular Formation of the Medulla Oblongata, Reacting to the Value of the Acceleration.

Out of the 110 neurons in the reticular formation of the medulla oblongata, 77 (70.9%) showed a reaction to the periodic change in the value of the acceleration. Examples of correlation functions of this type are shown in Figure 1.

The period of time for low-frequency oscillations was calculated according to Formula (3). The value for this period was 1.2-1.4 sec, which corresponds to the real period for the rocking.

For 18 neurons (16.3%), no reaction to acceleration (Fig. 2) was found.

15 neurons constituted a particular group of neurons called "doublets". The examination of their correlation function is the topic of a separate study. /203

In the visual region of the cerebral cortex, all the neurons being studied showd no reaction to the change in acceleration, and had correlation characteristics similar to those given in Figure 2.

Therefore, a change in the pulse rate during rocking is observed both in the reticular formation of the medulla oblongata and in the visual region of the cerebral cortex.

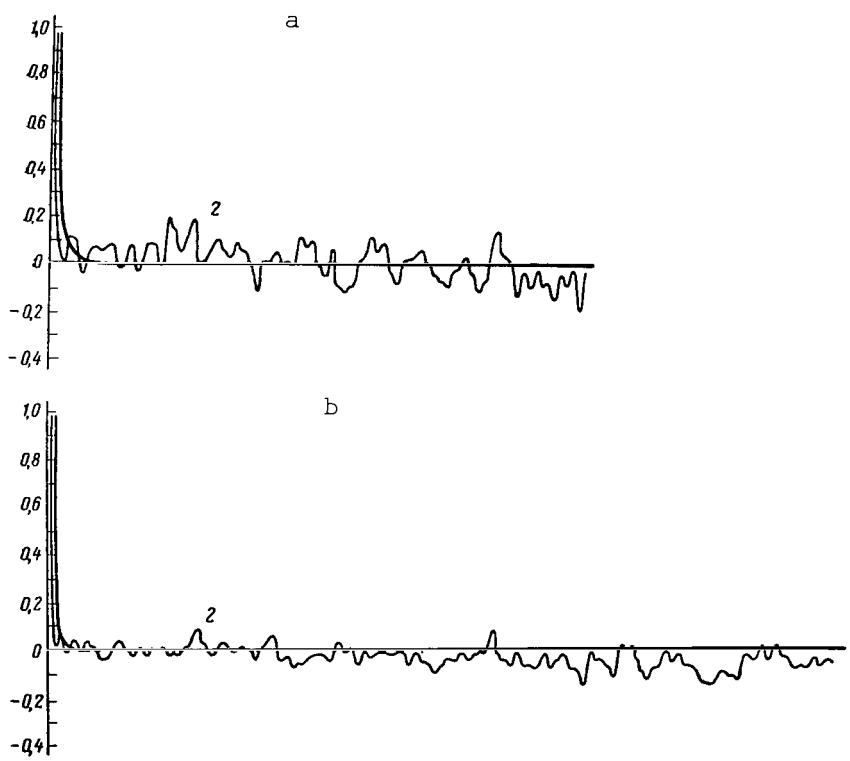

Fig. 2. Correlation Functions of the Intercommisural Intervals Which do Not React to Acceleration. (a) Visual Region of the Cerebral Cortex; (b) Reticular Formation of the Medulla Oblongata. Symbols as in Figure 1.

The use of correlation analysis allowed us to detect the difference in the reaction of neurons in the same regions, in relation to the change in acceleration. The neurons of the reticular formation in the medulla oblongata clearly showed a reaction to periodic changes in acceleration, while the neurons of the visual region of the cerebral cortex did not show any reaction to such a change. /204

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THE REACTION OF SINGLE NEURONS IN THE AUDITORY REGION OF THE CEREBRAL CORTEX IN CATS TO AN ADEQUATE STIMULATION OF THE VESTIBULAR APPARATUS

M.G. Kutateladze

ABSTRACT: The effect of adequate stimulation of the vestibular apparatus (rocking on a test-stand with an acceleration of 0.8-1.2 g) is examined for the activity of the neurons in the auditory region of the cerebral cortex. A microelectrode technique was used for recording from the neurons. The results obtained were processed by a method of correlation analysis. It was shown that despite the change in the frequency characteristic of the impulse activity in the neuron, the correlation characteristics did not show any relationship between the change in the activity of the neuron and the change in the value of the acceleration. Because of this, it was assumed that stimulation of the vestibular apparatus has a non-specific effect on the auditory region of the ceregral cortex.

The problem of the relationship between the vestibular and the auditory analyzers is of great interest when we consider their close phylogenic and anatomical relationships. However, there are only a limited number of sources examining the relationship between these analyzers in the literature. /204

Thus, G.L. Komendantov found that bone conduction changes [6] during stimulation of the vestibular apparatus.

A. Kh. Min'kovskiy, G.G. Aslanyan, and K.G. Shukuryan [1,7] obtained interesting data. These authors studied the marginal sensitivityof the auditory analyzer during stimulation of the vestibular apparatus. They found that a change in the sensitivity of the auditory analyzer depends on the development of negative or positive induction in the nerve centers. V. G. Bazarov [2] found that the vestibular-vegetative reactions are suppresed during the simultaneous effect of 2 stimulations (vestibular and auditory); as for the vestibular-secretory reaction, V.S. Nazarenko found that these reactions are intensified [8-10].

Electrophysiological examinations of the relationship between the auditory and vestibular analyzers were described in studies by G.I. Gorgiladze, Kornhuber and DaFonseca, and G.I. Gorgiladze and G.D. Smirnov [3,4,11]. It follows from these studies that

polarization of the labyrinth has a suppressing effect on the resultant responses (clicks) in the auditory cortex. The reaction of the neurons in the auditory cortex to stimulation of the vestibular apparatus, in the opinion of these authors, is non-specific.

Since we have indications that the cortical representation of /205
the vestibular apparatus is located in the auditory region of the cerebral cortex [12,13], we decided on doing research with the aim of studying the reaction of single neurons in this region as a response to adequate stimulation of the vestibular apparatus.

METHODS

The experiments were conducted on 26 adult cats (weighing 2.5-4 kg). The animal was anesthetized with ether and held in a stereotaxid device; tracheotomy and curarization (5 mg/kg of diplacin) followed, after which the animal was given artificial respiration.

A wide craniotomy permitted access to the cerebrum. [redacted] opening up the dura mater, the brain was bathed with warm mineral oil. In order to decrease the pulsation, we drained the cisterna magna and made a pneumothorax. The animal was then transferred to a dark chamber on an experimental stand, which allowed stimulating the otolith apparatus (vertical dislocation with linear acceleration of 0.8-1.2 g). The experiment began 1.5 hours after ether was administered and the animal was given artificial respiration.

The extracellular activity of individual neurons in the auditory region of the cerebral cortex was recorded with the aid of glass microelectrodes, whose diameter at the tip was 0.5-2 μ and which were filled with a 3-molar solution of KCl. For the recording, we used an alternating-current amplifier UBP 1-01, a "Sanei" oscillograph, and a MAG-8 tape recorder.

The data obtained were processed by determining the average frequency for the sequence of the commisures per second during various periods of the experiment (background, rocking, after rocking). Inasmuch as this method did not allow an accurate calculation of the nature of the changes in the neurons activity relative to rocking, we used a method of automatic correlation analysis (for development of this method, see page 211 in this volume). This method allows isolating the periodic signals from the noise background, thus establishing the relationship between the change in the recorded parameter (change in the value of the intercommisural interval) and the change in the value of the acceleration. In our case, rocking (change in acceleration) was the periodic signal. The calculations were made on the "Dnepr-1" computer.

RESULTS

We recorded and studied in detail, the activity of 74 neurons in the auditory region of the cerebral cortex. The neurons were recorded at a depth of 500-2000 μ.

Out of the 74 neurons recorded, 71 showed spontaneous activity, while 3 neurons were activated only during rocking. The rate /206
of impulses from the spontaneously active neurons varied from 0.5 to 30 imp/sec. The commisures, as a rule, had non-rhythmicity; they were both single-phase (negative or positive) and two-phase (negative-positive) in form.

After recording the background activity of the neuron, we produced 15 vibrations per 20 sec. It was found that the neurons in the auditory region of the cerebral cortex showed 4 types of reactions to the rocking.

Type I. An increase in the pulse rate (31.7%). Some of the neurons increased their activity to the maximum immediately (during the first second of the rocking) while others increased their activity gradually, reaching a maximum only 10-15 sec after the beginning of the rocking.

Type II. A decrease in the pulse rate (54%). Some of the neurons decreased their activity immediately at the beginning of the rocking. The others gradually decreased in activity.

Type III. The change in the pulse activity had a phase character. The increase in the pulse activity changed to a decrease in the rate; the pulse rate then increased again (9.3% of the neurons).

Type IV. These were neurons whose pulse activity did not show any apparent reaction to the rocking. There were 12.7% of such neurons.

Signs of adaptation were detected in 13 of the 74 neurons. They belonged to thse neurons whose reactions to the rocking were of both Types I and II. The adaptation appeared about 15-16 sec after the beginning of the rocking.

After termination of the rocking, some of the neurons continued to increase their activity (neurons of Types I and II), while others decreased it (neurons of Type II).

Analysis of the data by the correlation method showed that of the 74 neurons in the auditory region of the cerebral cortex, despite the quantitative changes in the pulse activity (increase or decrease during rocking), in no case did the correlation functions of the intercommisural intervals contain periodic components, i.e., the neurons in this region did not show any reaction to a periodic change in the value of the acceleration (Fig. 1a).

Thus, the data we obtained showed that adequate stimulation of the vestibular apparatus by rocking leads to a change in the rate of neuron pulse activity. However, in contrast to the data obtained in studying the correlation function of the inter-

commisural intervals in the neurons of the anterior suprasylvial gyrus, where we found characteristic changes in relation to the change in the value for the acceleration (Fig. 1b) (projected zone of the otolith apparatus), there were no such changes in the neurons of the auditory region. Naturally, if the correlation of the values /207
for the intercommisural intervals of the neurons in the auditory region does not change in relation to the change in the value of the acceleration, it becomes clear that the rocking causes non-specific reactions on the part of the neurons in the auditory region. We can assume that the impulses from the vestibular receptors go to the reticular formation of the brain stem or through the vestibular nuclei, and then, passing through the thalamic non-specific system and being distributed in a more or less random manner over the entire surface of the cortex, cause the reaction of the neurons in the auditory region.

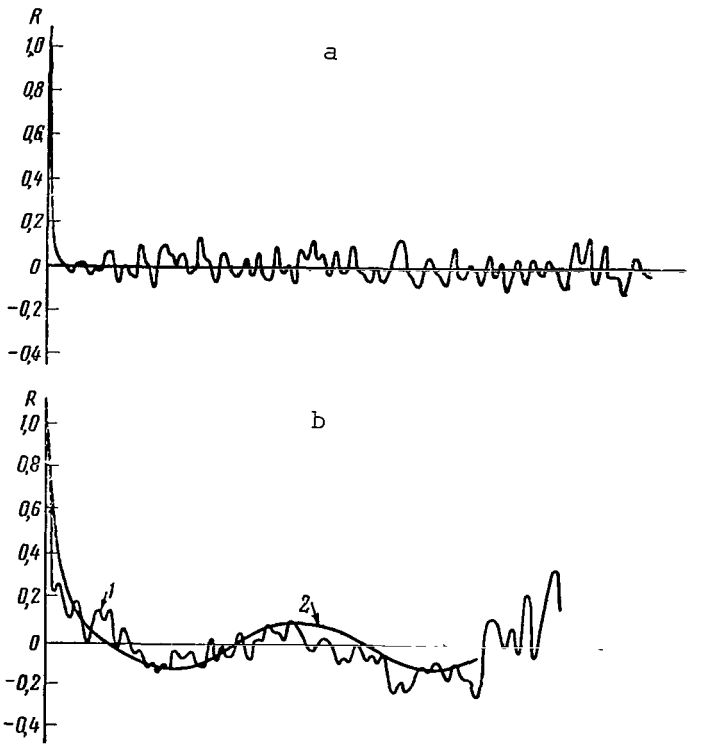

Fig. 1. Correlation Function of the Intercommisural Intervals which do Not React (a) and Do React (b) to a Change in the Value of the Acceleration. The Period of Time for Oscillation of the Correlation Function is 1.2 sec (Actual Time of Rocking). (1) Real Correlation; (2) Approximate.

On the basis of the results of this study, we can conclude /208
that adequate stimulation of the vestibular apparatus by rocking has a non-specific effect on the functional condition of the auditory region of the cerebral cortex.

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ACTIVITY OF INDIVIDUAL NEURONS IN THE RETICULAR FORMATION OF THE MEDULLA OBLONGATA (N. GIGANTOCELLULARIS) IN CATS DURING ROCKING

N. V. Merabishvili

ABSTRACT: The reactions of individual nerve elements in the reticular formation of the medulla oblongata (n. gigantocellularis) in cats are examined for an adequate stimulation of the otolith apparatus by rocking. A microelectrode technique was used for recording the potentials. The results were analyzed with the aid of a correlation analysis which indicated that the majority of the reticular neurons in question (85.6%) showed a specific reaction to a change in the value of the acceleration.

The examination of the functional relationships between the /208
vestibular nuclei and the reticular formation is of great significance for understanding the nature and mechanism of the shifts occurring during the effect on an organism produced by a change in the gravitational field [12,13].

An anatomical and physiological analysis of these relationships was undertaken by a number of authors [9-11, 13-22, 25]. However, we could never consider that this problem was completely solved.

The purpose of this study was to explain the nature of the reaction on the part of the neurons in the nucleus gigantocellularis of the reticular formation, to the effect of linear accelerations.

METHODS

The experiments were conducted on 20 anesthetized cats (40 /209
mg/kg of chloralose + 15 mg/kg of nembutal, intraperitoneally).

In order to preserve the structure of the parts of the central nervous system (the cerebellum, in particular), we gained access to the reticular formation of the medulla oblongata through the base of the cranium. The cats' heads were fixed in stereotaxic devices, with the occiput below (+90° according to Magnus).

The commisural activity of individual nerve elements was recorded extracellularly by glass microelectrodes; the exterior diameter of the tips was 1-2μ, and they were filled with a 3-molar solution of KCl. The microelectrodes were inserted in the n. gigantocellularis with the aid of a hydraulic manipulator using

the Sentogotai coordinates at a point 45° $a5$, $a3$, $a1$.

In order to identify the group of reticular neurons to which these neurons belonged, we used their particular reactions to afferent pulses of varying modality [7,21]. For this purpose, we placed stimulating electrodes on the sciatic nerve. The nerve was stimulated by a square-wave generator (single or paired pulses lasting up to 0.2 msec). The pulses had amplitudes up to 10 V.

The reliability of the electrode location in this nucleus was determined with a microscope after fixing the brain in formalin and staining the frozen sections with hematoxylin-eosin.

The respirational and cardiovascular pulsations were decreased by adding agar-agar [37°) [8].

The pulse from a single neuron was recorded on magnetic tape through an alternating-current amplifier UBP1-01, with subsequent recording on photographic film with the aid of a dual-beam oscilloscope (EMOF2-01).

The animals and the stereotaxic device were mounted on a special test-stand; vertical displacements of the animal were made at accelerations from 0.8-2 g [4].

This method permitted stimulation of the otolith section of the vestibular apparatus [1-3, 5, 5, 19, 23, 24].

An analysis of the reaction of the neurons to rocking was done by two methods: (1) a preliminary analysis was made by calculating the number of impulses per 1/2 sec, and by averaging the data obtained for 20 sec before the effect, during the rocking, and after termination of the stimulation; (2) for a more accurate evaluation, we used the method of correlation analysis, which permitted isolating the periodicity of the signals against the noise background (for the method of using correlation analysis, see p. 211 in this Volume).

RESULTS

Of the 125 neurons, 19 (15.2%) had no spontaneous activity, /210
and were activated during the rocking. A substantially greater number [91 neurons (72.8%)] had spontaneous activity which varied from 0.4 to 5 imp/sec. The frequency for the sequence of the commisures, 1-29 imp/sec, was found more frequently.

We observed the following forms of spontaneous activity: rhythmic, arrhythmic, transitional, and dual commisure-doublets.

According to their form, the commisures were classified as follows: single-phase; negative or positive and two-phase; positive-negative.

In their response to stimulation of the otolith apparatus by rocking, the neurons in the nucleus gigantocellularis of the reticular formation were found to have three types of reactions.

Type I: 62 neurons (49.6%), whose increase in activity did not occur in a uniform manner: some changed the pulse rate periodically, others had a two-phase change in activity, and, finally, there were those neurons which showed a gradual increase in activity.

24 neurons (19.2%) showed an increase in activity during the first seconds of the rocking (6-7 sec). This increase then changed to a decrease within 4-5 sec. Beginning with the 10-12th second, there was a secondary increase in frequency, and then a decrease, etc. Such a change in the frequency for the sequence of commisures had a periodic character. However, the average increase in the activity during this decrease exceeded the background pulse rate. The pulse rate increased roughly twice.

After the stimulation was stopped, a return of the background activity was observed from the very first second. However, a complete recovery was found only 3-4 seconds afterwards.

The next group consisted of 19 neurons (14.4%). Their activity increased up to a certain level during the first second of the rocking, and remained there for 4-5 sec; there was then a further gradual and progressive increase from the 5th second. It was found that the activity increased with every second of the rocking, and reached its maximum at the 17-18th second, after which it became stable and did not change its character until the end of the rocking. The pulse rate increased by a factor of two.

The neurons of the latter group differed in their pronounced sequential reaction. After the rocking, the activity continued to increase and the pulse rate was 10-15% higher than during the period of rocking.

Let us turn now to an examination of the neurons of Type II, whose activity decreased during rocking. There were 39 such neurons found (31.2%). In relation to the character of the rhythm for the sequence of the commisures, these neurons could be subdivided into 2 subgroups: those neurons which preserved their rhythmicity, and those neurons whose rhythms for the sequence of the commisures changed.

For 27 neurons (21.6%), there was a sharp retardation of the activity by 2-3 imp/sec from the very first second. Around the 5-6th second, on the contrary, there followed an increase in the activity; at the 16th second the pulse rate returned to the level corresponding to background data. /211

The other subgroup consisted of 12 neurons (9.6%). At the beginning of the rocking, the pulse rate did not change for

3-4 sec; then, from the 5th second to the 11-12th, there was complete retardation. Subsequently, there appeared activity of high frequency, after which (from the 15th second to the end of the rocking) there was a gradual decrease in activity. The pulse rate decreased roughly by a factor of two.

Type III: Five neurons did not show any apparent reaction to the otolith stimulation. Therefore, the reaction of the neurons to the adequate stimulation of the vestibular apparatus by rocking proved to be very indefinite.

At the same time, considering that the method used for stimulating the vestibular apparatus (a change in the rectilinear acceleration during rocking) acts in accordance with the periodic law, and considering that the intercommisural intervals had random values, we could expect that analysis would be useful for determining which neurons react specifically to a change in acceleration. The presence in the correlation function of the intercommisural intervals, with periodic components and periods equal to the period of the rocking, shows the reaction of a given neuron to a periodic change in acceleration.

The correlation analysis divided the 125 neurons under study into 5 groups.

Group I (18 neurons, 14.4%). The correlation function of these neurons does not contain any periodic components, and it suggests a correlation function of a random signal (Fig. 1,I). We can assume that the neurons in this group do not react to a change in the value of the acceleration.

Group II (77 neurons, 70.9%). The correlation function for the neurons in this group (Fig. 1,II) contains periodic components, with periods equal to the periods of the rocking. Such a correlation function can easily be approximated by the formula $R(\tau) = Ae^{-\alpha\tau} \cdot \cos \omega\tau$. Such a type of correlation function indicates that /212 the neurons in a given group react linearly to a change in acceleration.

Group III (16 neurons, 12%). The correlation function of these neurons seems to show a combination of two frequencies (Fig. 1,III). We can give two very simple explanations for the origin of such a correlation function: (1) the neurons of this type represent simple integrators of two signals coming from the neurons of the second group which are linked with them, while the frequencies of these neurons differ from one another during the period of the rocking; (2) the neuron being studied represents a non-linear converter of the frequency, or, in other words, converts the frequency of the rocking to a higher frequency. We should note that such neurons as the dual commisure-doublets mainly belong to this group.

Both hypotheses naturally require further explanation.

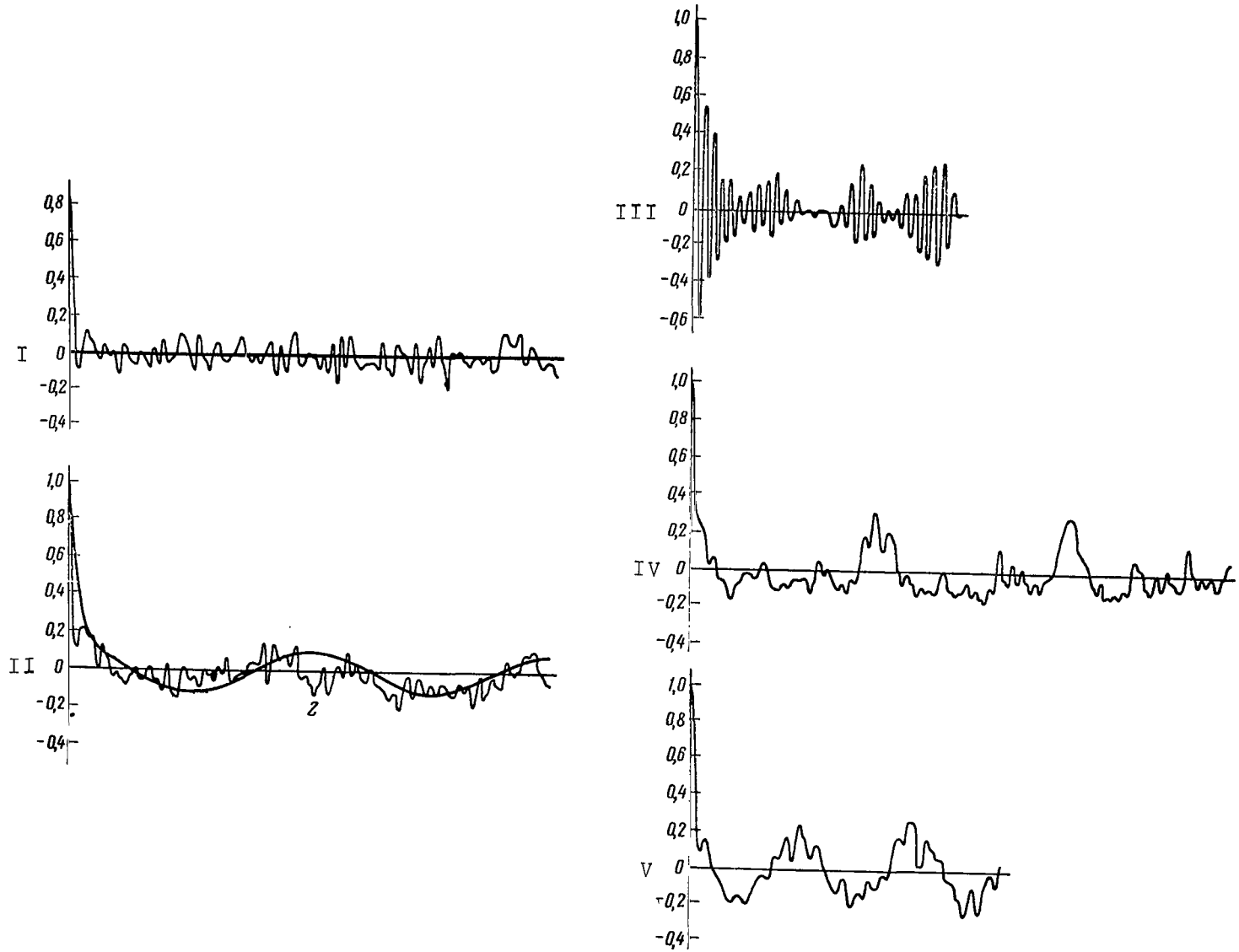

Fig. 1. Correlation Functions of the Intercommisural Intervals for the Neurons in the Nucleus Gigantocellularis of the Reticular Formation. I,II,III,IV, and V are the Groups; (1) Approximate; (2) Real Correlation.

Group IV (8 neurons, 6.4%). Bursts which are separated from one another by small negative values are characteristic of the correlation function of the neurons in this group, (Fig. 1,IV). The distances between the bursts are equal to half the period of the rocking. Such a correlation function can be obtained from a random sequence of numbers in which groups of numbers which differ sharply in value from the others are included at an even interval. This means that the given neuron reacts specifically only to individual values of acceleration. We can assume that these bursts coincide in time with the moment of the transition of the acceleration through zero. /214

Group V (7 neurons, 5.6%). For the correlation function of these neurons, the presence of periodic components with a period equal to the period of the rocking is characteristic (Fig. 1,V). In contrast to the neurons in Group II, the correlation function begins with a negative half-wave. On the basis of the theorem of summation of the correlation functions, we can assume that it is the sum of the correlation functions for the neurons in Groups II and IV. Therefore, in our case, the neuron which gives such a correlation function also reacts to a change in the value for the acceleration and to some concrete value of the acceleration. (According to our assumptions, g = 0 is such a value.

We considered the neurons for all the groups, excepting Group I, as reacting specifically to a change in acceleration. They make up 85.6% of the neurons being examined in the region of the nucleus gigantocellularis of the reticular formation of the medulla oblongata.

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THE EFFECT OF ADAPTATION TO DECREASED PARTIAL PRESSURE OF OXYGEN ON RESISTANCE TO ACCELERATIONS

P.V. Vasil'yev and N.N. Uglova

ABSTRACT: White mice, rats, guinea pigs, and rabbits were used in the experiments. In order to evaluate the organism's functional condition before and after training for hypoxia, the quantity of erythrocytes and hemoglobin and the level of the gas metabolism were determined. In a number of experiments, the electrocardiograms and pneumograms were recorded before, during, and after rotation. The quantity of erythrocytes and hemoglobin increased after adaptation to hypoxia; the oxygen requirement did not change substantially. The survival rate for the adapted animals during the effect of the accelerations was 24-46% higher than for the control animals. The increased resistance was retained for two to three weeks.

The search for an effective means of increasing an organism's /215
resistance to accelerations has acquired particular importance in view of the rapid progress in aviation and flights in spacecraft.

On the basis of the principal pathogenetic mechanisms for the effect of accelerations, the means and methods for increasing resistance are being developed in the following ways: production of anti-G suits; designing of special seats, which give an astronaut an optimum position in relation to the vector of accelerations; respiration under increased pressure; immersion systems of various types; physical training and general hardening of an organism, for pilots and astronauts; special training in a centrifuge; increasing an organism's resistance by applying pharmacological means with varying directions of the effect.

Each of these methods has its advantages and disadvantages. /216
Naturally, in looking for means and methods of increasing resistance, preference is given to those which do not require complex and cumbersom installations, and are simple for testing, inexpensive, effective, and widely accessible.

Directed by these principles, we must first of all study the intrinsic possibilities of the organism itself, training and stimulating its compensatory mechanism. These purposes can be used for general physical training, training on a centrifuge [9,18], non-specific types of training and adaptation [6,16], and application of pharacological substances [2-4, 13, 14, 19-21]. Despite

the fact that a number of these methods are already being employed, their seientific basis is clearly insufficient.

The concepts of N.N. Sirotinin [16] on the possibility of using acclimatization to high-mountain conditions, as well as on a non-specific method for increasing resistance to accelerations, are of definite interest. This concept was confirmed in experimental studies by V.P. Dudarev [6]. This author showed that the survival rate of acclimatized white rats, in particular, was 30% higher than for control animals. Practical problems urgently need further expansion of these initial studies.

The purpose of this article is to study the effect of various methods of adaptation on animals' resistance to accelerations, and to determine the periods of time required for the animals' readaptation. This article is the first of a series of studies.

METHODS

The experiments were conducted on 571 white mice, 99 white rats, 22 guinea pigs, and 6 rabbits.

Each series consisted of an even number of control (intact) and experimental (adapted to rarefied atmosphere in a pressure chamber) animals.

The length of time for adaptation varied from 3 to 14 days. The maximum degree of rarefaction reached 307.87 mm Hg, which corresponded to an altitude of 7000 m above sea level.

In order to evaluate the animals' functional condition before and after training for hypoxia, we determined the amount of erythrocytes and hemoglobin and the level of the gas metabolism in terms of the oxygen requirement in some of the animals.

The necessary values for the transversely-directed accelerations were reproduced in a centrifuge with a radius of 4.2 m for the white rats, guinea pigs, and rabbits, and in a centrifuge with a radius of 4.7 m for the white mice. In relation to the type of animal and the character of the experiment, we used accelerations with values varying from 12 to 45 units. The gradient of increase and decrease of an acceleration was 1 unit/sec.

In a number of experiments, we recorded the electrocardiograms /217 using standard leads I and II; the pneumograms were recorded on a pneumograph made by the "Elema" firm (Type 42-V) before, during, and after rotation. The animals were fastened in compartments on their backs and placed in the centrifuge, one control animal per container, with another experimental animal in the opposite container. In those experiments when the physiological functions were not recorded, the rotation was performed with plywood cases divided into sections; one animal was placed in each section.

The tolerance to accelerations was determined for the mice on the basis of a comparison of the survival rate for the experimental and control groups.

For the other types of animals, in addition to the survival rate, we analyzed the changes in the electrocardiographs and respiration, which showed the time of onset and the degree of the disorders in the functions of the cardiovascular and respiration systems.

When possible, all the experimental materials were subjected to a mathematical analysis, with calculation of the average arithmetic values (M), the average error (m), and the degree of reliability in the differences of the values obtained (T)[5,7,11].

EXPERIMENTS ON WHITE MICE

The mice were divided into several series in relation to the length of time for adaptation, and the time of the year (Table 1).

TABLE 1. DISTRIBUTION OF THE ANIMALS ACCORDING TO THE SERIES OF EXPERIMENTS, THE TIME THE EXPERIMENTS WERE CONDUCTED, AND THE PERIODS OF TIME FOR ROTATION IN THE CENTRIFUGE.

Series	Adaptation: Time of Experiment	Adaptation: Length of Time, Days	Number of Animals: Control	Number of Animals: Experimental	Number of Animals Subjected to Rotation in the Centrifuge After Termination of Adaptation: During the 1-5th days	During the 6-10th days	During the 11-18th days
I	Oct.	14	60	80	40/40	20/20	0/20
II	Dec.	14	21	20	21/20	---	--
III	Feb.	14*	40	40	20/20	20/20	--
		14**	40	40	20/20	20/20	--
IV	March	14	79	91	20/20	20/20	39/51
V	April	3.5	30	30	30/30	---	--

* Preliminary Adaptation
** Repeated Adaptation

In the first four series, adaptation was accomplished according to a single method which consisted of daily 6-hour sessions at high altitudes: the first day, at an altitude of 3000 m, the second and third days, at an altitude of 4000 m, the fourth day, at an altitude of 4500 m, the fifth to seventh days, at an altitude of 5000 m, the eighth day, at an altitude of 5500 m, the ninth day, at an altitude of 6000 m, the tenth and eleventh days, at an altitude of 6500 m, and the twelfth to fourteenth days, at an altitude of 7000 m. /218

The animals of Series V remained at the same altitude continuously for 3.5 days, and the graph for the after effects of the climbs remained the same as during the 14-day adaptation.

During adaptation, the moisture content in the pressure chamber remained at a level of 50-70%, and the temperature at 25-27°. The conditions for removal and feeding were the same for all groups of control and experimental mice.

At the end of the adaptation time, we could not find any differences between the experimental and control mice by an external examination: they all reacted in a lively manner to external stimuli (pain, sound), they were active and willingly ate their food, and their fur was smooth and shiny. The weight of the experimental mice, as a rule was somewhat less than that of the control mice.

Thus, for example, an examination of the animals in Series IV after the termination of adaptation showed that the control mice gained more weight, by a factor of 2 or 3, than the experimental mice.

It is now well known that the organisms of animals and men respond to oxygen deficiency in the inspired air by a number of adaptation reactions intended for preservation of homeostasis. Many researchers, native and foreign, have studied these reactions.

In relation to this, it has been shown that, if intensification of the pulmonary ventilation and an increase in the minute volume of the blood are mainly characteristic of the first period of adaptation, then an increase in the amount of erythrocytes and hemoglobin appears later, in a gradual reaction which lasts for a long period of time.

In our experiments, we determined the amount of erythrocytes and hemoglobin before adaptation, and also during the third and seventh days after termination of adaptation (Table 2).

From the data presented, we can see that the quantity of erythrocytes and hemoglobin in the white mice was within the limits of the type-norm before the experiment [15]; the number of red blood corpuscles varied from 8240 to 8620 thousand, and the amount of hemoglobin varied from 12 to 14 g%.

After adaptation according to the method described, there was an increase in the number of erythrocytes on the third day (an average per group of 3500 thousand), and an increase in the amount of hemoglobin by 5 g%. Blood analyses, conducted on the seventh day after termination of adaptation, showed a certain decrease in the characteristics being studied, in comparison with previous studies.

Other authors also observed similar changes in hemopoiesis

during adaptation to hypoxia [6,16].

In addition to studying the characteristics of the red blood, we determined the level of the oxygen requirement in 10 mice in a given series of experiments, before adaptation as well as on the first and sixth days after the termination of adaptation (Table 3). /219

TABLE 2. AMOUNT OF ERYTHROCYTES (PER THOUSAND) AND HEMOGLOBIN (PER g%) IN THE BLOOD OF WHITE MICE BEFORE AND AFTER ADAPTATION.

Before Adaptation		After Adaptation			
		Third Day		Seventh Day	
g%	Thousand	g%	Thousand	g%	Thousand
13,2	8620	17	11250	—	—
13	8610	19	11220	17	11770
14	8240	18	10630	15,8	10220
13,2	8610	18	12680	17	9900
13,8	8240	19	12900	17	13000
12,4	8470	19	12080	15,6	9240
13	8390	17	13000	17,4	10140
12	8540	16	11520	15,6	10050
$M \pm m$	13±0,42	8465±568	18±0,4	11910±316	16,5±0,3	10620±490
T	—	—	8,1	10,9	6,6	4,38

As we can see, during the first few days after adaptation, the level of the oxygen requirement in the mice remained unchanged in comparison with the control studies. During the following determination, we observed a slight increase (by 14%) in the gas exchange, which can hardly be linked with the preceding adaptation.

TABLE 3. DYNAMICS OF OXYGEN REQUIREMENT IN THE MICE BEFORE AND AFTER ADAPTATION TO HYPOXIA (AVERAGE PER GROUP OF 10 MICE).

Time of Determination	Total Weight of the group, g	Total Requirement in 15 min	Requirement ml/kg in 1 min
Before Adaptation	192	210	72.8
After Adaptation:			
First Day	208	225	72.12
Sixth Day	219	280	82

In order to determine their resistance to accelerations, the animals were rotated in the centrifuge for various periods of time after the termination of training in the pressure chamber. /220

In this case, we did not note any significant differences in the survival rate of the mice in different series for identical periods of adaptation, (Table 4).

TABLE 4. SURVIVAL RATE OF THE WHITE MICE WHICH WERE ADAPTED TO HYPOXIA, DURING THE EFFECT OF ACCELERATIONS (45 UNITS).

(Composite Date According to Series I-IV of the Experiments)

Group Number	Group	Days After Adaptation	Total no. of mice	Result		Survival Rate, %	Degree of Reliability
				Died	Survived		
1	Control	1—5-e	101	66	35	34,6	—
2	Experimental		100	32	68	68	5
3	Control	6—10-e	60	31	28	46,6	—
4	Experimental		60	22	38	63,4	1,87
5	Control	11—18-e	39	25	14	35,9	—
6	Experimental		71	35	36	50,5	1,52

We can see from the data presented that an acceleration of 45 units (twice in 10 min, with an interval of 10 min between each rotation) resulted in death for the control mice in more than half of the cases. The animals which survived for serveral minutes to several hours were in a state of hypodynamia and general inhibition. Their reactions to sound signals and pain stimuli were sharply reduced. In this case, we did not find any difference between the adapted and control mice during this period (as determined according to the general methods of clinical observation). The period for recovery of the physiological functions lasted for the same period of time.

In comparing the data for the survival rate in the experimental and control groups, we can see that the adaptation had a pronounced positive effect.

In this case, the most favorable results were found for rotation during the first five days after adaptation. During this time, the survival rate in the experimental group was twice as great as in the control group. In the examinations during the sixth to tenth days, the effect (although it decreased somewhat) remained very pronounced positive effect.

In this case, the most favorable results were found for rotation during the first five days after adaptation. During this time, the survival rate in the experimental group was twice as great as in the control group. In the examinations during the sixth to tenth days, the effect (although it decreased somewhat) remained very pronounced. The results of a statistical analysis show that in both cases the difference in survival rate between the experimental and control groups was significant, and the probability of error did not exceed 0.1% in the first case and 5% in the second case.

During the following days, the resistance of the adapted mice /221
continued to decrease. Actually, if the survival rate in the experimental group reached 68% during the first five days, and 63.4% during the sixth to tenth days, then it would be 50.5% in all during the eleventh to eighteenth days. It is true that it still exceeded the survival rate of the control groups, but the difference was already statistically unreliable (T = 1.52).

Subsequently, we can see from an analysis of the results of these experiments that adaptation to decreased barometric pressure was accompanied by a significant increase in the resistance of the white mice to the effect of accelerations; the duration of the increased resistance for the animals lasted for 2-3 weeks.

An examination of the results of the experiments with repeated adaptation is of definite interest.

Experiments were conducted in February on 110 animals which were divided into three groups. The first group included 39 animals which had already been subjected previously to 14-day adaptation to hypoxia. The interval between the preliminary and repeated adaptations was 41 days. All during this time, the mice were kept in a vivarium. The second group included 40 preliminarily-adapted mice. Finally, the third group were the controls.

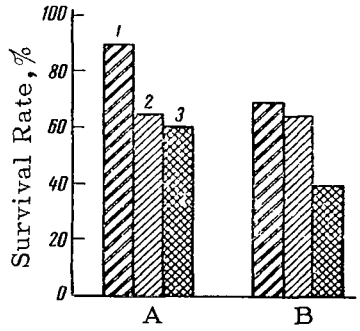

Fig. 1. Survival Rate of Mice During Rotation in a Centrifuge on the Second (A) and Ninth (B) Days After Adaptation. (1) Preliminary Adaptation; (2) Repeated; (3) Control.

The type of adaptation to hypoxia, the temperature, and the moisture content in the pressure chamber were the same during this experiment as during the previous experiments.

After 14 days of adaptation, the condition of all the animals was satisfactory. However, both experimental groups lost weight. The total weight of the first group before adaptation was equal to 1145 g; immediately after adaptation, it was 1050 g., i.e.,the losses in weight consisted of 95 g (8.4% of the original weight).

The mice which had been adapted for a second time weighed 1150 g before the experiment and 110 g afterward, i.e., they lost 50 g in weight, which consisted of 4.35%. The group of control animals gained 200 g in weight during the same period, i.e., 14%.

The resistance to accelerations was determined during the second and ninth days after adaptation (Fig. 1).

In examining the results presented, we can see that the positive effect appeared more clearly on the second day for the group which had been adapted twice. The survival rate in this group was 30% higher than in the controls. Statistically, this difference is reliable in comparison with the survival rate in the control group (T = 2.3). /222

The effect of preliminary adaptation was insignificant for rotation during the second day in this experiment, and the survival rate for the second group differed from the survival rate in the control by 5% in all.

During the rotation on the ninth day, the survival rate in the second group remained the same as in the previous experiment, while it decreased by 22% for those in the first group.

We have the impression that repeated adaptation to decreased barometric pressure is accompanied by a more significant increase in resistance to the effect of accelerations than for initial adaptation.

Thus, remaining in a pressure chamber for 6 hours, every day for 14 days, resulted in a clearly pronounced increase in the resistance of the mice to the effect of accelerations.

We were tempted to shorten the period of time for adaptation by means of continuous training for 84 hours, keeping the mice at a certain altitude for a shorter period of time, for which we established Series V of the experiments (100 white mice).

The mice were trained in a pressure chamber in the following way: 6 hours at an altitude of 3000 m, 12 hours at an altitude of 4000 m, 6 hours at 4500 m, 12 hours at 5000 m, 6 hours at 5500 m, 6 hours at 6000 m, 12 hours at 6500 m, and 18 hours at 7000 m. This corresponded to 6 hours of the effect for 14 days.

The animals were rotated in the centrifuge on the second and fourth days (Table 5).

TABLE 5. SURVIVAL RATE OF THE MICE DURING THE EFFECT OF ACCELERATIONS AFTER REMAINING CONTINUOUSLY IN A PRESSURE CHAMBER FOR 84 HOURS

Group Number	Group	Day After Adaptation	Number of Mice	Result		Survival Rate, %	Degree of Reliability, T
				Died	Survived		
1	Control	Second	15	10	5	33.3	--
2	Experimental		15	8	7	46.6	0.72
3	Control	Fourth	15	9	6	40	--
4	Experimental		15	9	6	40	0

We can see from Table 5 that the survival rate in the control group was 13% lower on the second day than in the experimental group. However, in a mathematical analysis, the difference was found to be unreliable (T = 0.72).

On the fourth day, there was no difference in the survival rates. Therefore, we did not find any positive effect for the characteristics of resistance to accelerations for this type of adaptation.

EXPERIMENTS ON WHITE RATS /223

We examined 99 white rats (males, weighing 140-180 g).

The conditions for keeping and feeding the animals in the control and experimental groups were identical. The control rats gained weight during the adaptation, roughly 22.4% more than the experimental animals.

Investigations of the amounts of erythrocytes and hemoglobin were made on 6 rats before adaptation, as well as on the first and seventh days after the adaptation, (Table 6).

It follows from Table 6 that, before the adaptation of the white rats, theamount of erythrocytes varied from 6690 to 7590 thousand, and the amount of hemoglobin varied from 13.4 to 15 g%. On the first day after termination of adaptation, the number of erythrocytes (average per group) increased by 910 thousand, and the amount of hemoglobin increased by 1.4 g%. On the seventh day, these differences were found to be even somewhat higher.

For the same six rats, we determined the level of the gas exchange, before and on the first day after adaptation. The animals were placed in the chamber in pairs. In both cases, the pairs consisted of the same rats.

TABLE 6. AMOUNTS OF ERYTHROCYTES (PER THOUSAND) AND HEMOGLOBIN (PER g%) IN THE BLOOD OF WHITE RATS BEFORE AND AFTER ADAPTATION.

No. of animals	Before Adaptation		After Adaptation			
			First Day		Seventh Day	
	g%	Thous.	g%	Thous.	g%	Thous.
1	13'4	7480	16,6	8040	15	—
2	15	7400	16,4	8670	15,2	8900
3	15	6830	16,2	8720	16	7820
4	13,4	6690	14,5	7930	15,4	9050
5	14	7590	16	6900	14	7530
6	14,6	7060	15,4	8300	15,4	8900
M	14,07	7180	16	8090	15,24	8440

However, the increase in the level of the oxygen requirement observed in them on the first day after the adaptation was unreliable.

We determined the effect of adaptation on the resistance to accelerations on the 1-5th, 6-10th, and 11-16th days after adaptation (Table 7).

We can see from the data presented that, on the 1-5th days, the survival rate in the experimental group exceeded that in the control by a factor of almost two. On the 6-10th days, the positive effect proved to be even somewhat higher. The difference in survival rates between the control and experimental animals was equal to 43%. The results of the rotations imposed on the 11-16th /224 days show complete disappearance of the positive effect of adaptation to hypoxia on the animals' tolerance to accelerations.

TABLE 7. SURVIVAL RATE OF THE RATS WHICH WERE ADAPTED TO HYPOXIA, AFTER THE EFFECT OF ACCELERATIONS

Group Number	Group	Days After Adaptation	Total Number of Rats	Result		Survival Rate, %
				Died	Survived	
1	Control	1-5th	28	21	7	25
2	Experimental		37	20	17	46
3	Control	6-10th	7	6	1	14
4	Experimental		7	3	4	57
5	Control	11-16th	10	7	3	30
6	Experimental		10	7	3	30

The rats' tolerance to accelerations was determined, not only by the survival rate, but also by the data from the electrocardiographs and respiration. The recordings were made for 9 control and 9 experimental animals before, during, and after rotation in the centrifuge. The amount of the acceleration was increased intermittently, with an interval of 5 units and a rate of increase of 1 unit/sec. At each state of the acceleration (5,10,15 units, etc), we made a "plateau" for 1 min. At the end of the plateau, we recorded the electrocardiograms and the respiration for 10-15 sec.

Fig. 2. Pulse Rate for Rats During the Effect of an Acceleration, Increasing Stepwise. (1) Experiment; (2) Control.

In analyzing the materials obtained, we notice in particular that, out of the 18 animals, a compensatory increase in the rate of the cardiac activity was observed only in 4 rats (3 control and 1 adapted). The tachycardia in this case did not exceed 2-7%; as a rule, this was observed during accelerations which were not higher than 20 units (Fig. 2). /225

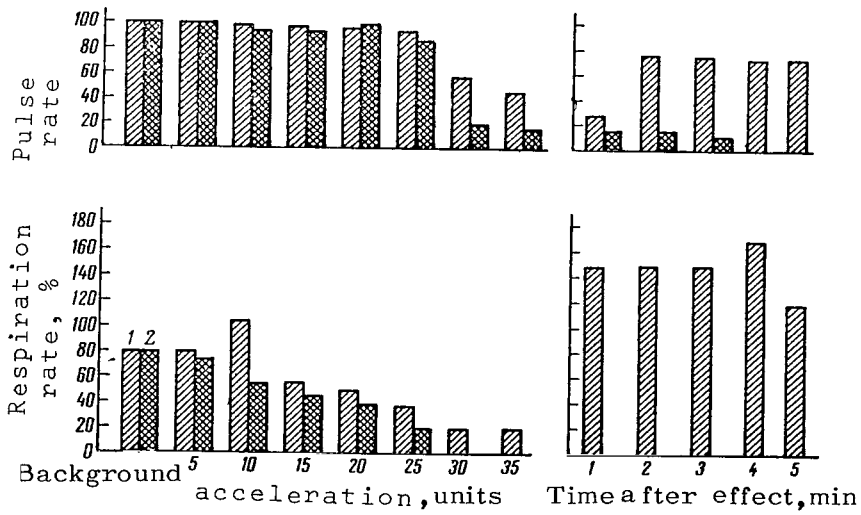

Fig. 3. Pulse Rate and Respiration Rate for Rats During the Effect of Accelerations Increasing Stepwise. Symbols as in Figure 2.

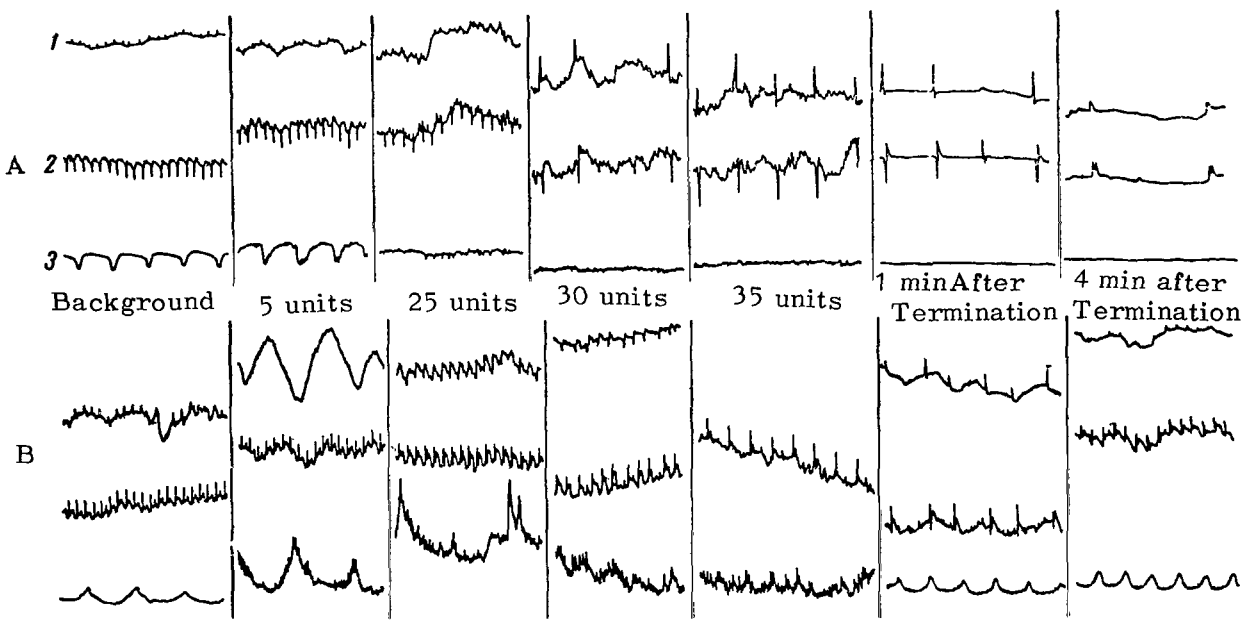

Fig. 4. Electrocardiograms and Respiration for a Control (A) and an Adapted (B) Rat During the Effect of Accelerations. (1) Electrocardiogram, Ist Lead; (2) Electrocardiogram, IIIrd Lead; (3) Respiration.

In 8 animals, even during an acceleration of 5 units, there was a decrease in the pulse rate, which subsequently progressed at a varying rate. A sharply-pronounced bradycardia, indicating developing decompensation, was observed in most of the rats during accelerations of 3 - 34 units (Figs. 2 and 3); in some animals it was seen clearly even during accelerations of 15 units.

In nearly every experiment, bradycardia appeared earlier and in a more pronounced form for the control rats (Figures 2 and 3). On the electrocardiograms, a change in the intervals of the R-R waves and in their amplitudes (Fig. 3) was very apparent, and also appeared only during accelerations of more than 25 - 30 units. However, in some animals we did not notice any pathological changes on the part of the elements in the electrocardiograms, even during accelerations of 40 units. For the animals which did not survive, the rate of heart contractions toward the end of the rotation was 10-19% of the original, and for those which did survive, it was 18-22%.

The cardiac activity was recovered gradually. Only in two out of 18 experiments did the pulse rate come close to the norm in about 4 min; in all the other cases, the recovery time was longer than 10 min.

Therefore, there was also a definitely high resistance for the /227 adapted animals to the effect of accelerations according to the data from the electrocardiographs.

At the beginning of the rotation, there was a compensatory intensification of the respiration, which was expressed either by an increase in frequency or depth, or by a combined increase in both parameters (Fig. 4). During an acceleration of 15 - 20 units, there developed a complication in the respiratory movements, and this was often indicated by a straight line on the curves (Fig. 3).

During the recovery period, there was a clearly-pronounced compensatory dyspnea in most cases. We did not find any significant differences in the change of respiration between the control and experimental animals.

EXPERIMENTS ON GUINEA PIGS AND RABBITS

We used 22 guinea pigs (males) weighing 310-350 g and 6 rabbits (males) weighing from 2880 to 3050 g in the experiments; of these, 11 guinea pigs and 3 rabbits were adapted to hypoxia under the conditions of a pressure chamber.

During the study period, the control guinea pigs gained 11.3% more weight than did the experimental ones. As for the rabbits, the adapted animals lost 5.1 to 12% more weight (Table 8).

TABLE 8. WEIGHT OF GUINEA PIGS AND RABBITS BEFORE AND AFTER ADAPTATION (AVERAGED DATA)

Animals	Group	Weight, g		Change in Weight	
		Before Adaptation	After Adaptation	Absolute, g	% of Original
Guinea Pigs	Control	320	350	+60	+18.8
	Adapted	321	345	+24	+ 7.5
Rabbits	Control	2960	3200	+240	+ 8.1
	Adapted	2916	2683	-233	- 8

In order to evaluate the method used for adaptation of the experimental animals, we determined the amount of erythrocytes and hemoglobin. The studies were conducted on 6 guinea pigs and 3 rabbits before adaptation and on the second and seventh days after adaptation (Table 9).

In comparing the resutls obtained, we can see that, after the termination of adaptation, the amount of erythrocytes in the guinea pigs increased during the studies on the second day by 630,000, and on the seventh day, by 810,000. The amount of hemoglobin remained practically the same. /228

For the rabbits, the increase in the number of red blood corpuscles was by 490,000 and 1,870,000, respectively.

TABLE 9. AMOUNT OF ERYTHROCYTES (PER THOUSAND) AND HEMOGLOBIN (PER g%) IN THE BLOOD OF THE ANIMALS BEFORE AND AFTER ADAPTATION.

No. of animals	Before Adaptation		After Adaptation, days			
			Second Day		Seventh Day	
	g%	Thousand	g%	Thousand	g%	Thousand
Guinea Pigs						
1	12	6050	13,4	6920	14	7080
2	13	5640	13,5	6180	13,2	6860
3	15	6540	14,9	6490	15,2	6380
4	14	5720	14,4	6570	14,6	7610
5	14	6430	15,4	6730	16	6370
6	14,4	5670	13,4	6980	15	6600
$M \pm m$	13 7±0,44	6010±160	14,1±0,35	6640±120	14,7±0,40	6820±185
T	—	—	0,7	3,30	1,7	3,4
Rabbits						
1	12	4690	14	5560	15	5500
2	13	4500	13	5300	14	7180
3	13	4900	13,5	4700	15	7020
$M \pm m$	12,8±0,49	4700±115	13,5±0,09	5190±255	14,7±0,11	6570±535
T	—	—	3,9	1,75	10	3,43

We determined the level of the gas exchange according to the O_2 requirement in 3 pairs of guinea pigs, 15 min before the experiment and on the first and sixth days afterward (Table 10).

During rotation in the centrifuge, 8 out of 11 adapted guinea pigs survived, and 3 of the controls survived. Therefore, the survival rate in the experimental guinea pigs was 45.7% higher. Out of the 6 rabbits (3 control and 3 experimental) subjected to the effect of accelerations, only 1 survived; the latter had been adapted to conditions of hypoxia.

As was the case for the rats, the tolerance of the guinea pigs and rabbits was determined according to the electrocardiographs and respiration.

The compensatory increase in the rate of the cardiac activity was more clearly pronounced in the guinea pigs than in the rats. This was observed in 14 out of 22 animals. This increase in the rate, as a rule, was noted in the control animals during accelerations which were not higher than 5 - 10 units, and in the experimental animals during stresses up to 15 units. Bradycardia /229
then appeared, with varying intensity: for most of the experimental guinea pigs, during an acceleration of 20 units; for the control animals, during an acceleration of 10 - 15 units (Fig. 5). Subsequently, the onset of bradycardia appeared sooner and more sharply in the control guinea pigs.

The cardiac activity was recovered rather slowly. In most cases, the recovery time exceeded 10-25 min.

A clearly-pronounced respirational arrhythmia was noted in both control and experimental animals.

In addition to the reaction on the part of the cardiovascular system, there was a compensatory intensification of respiration at the beginning of the effect of the accelerations, which appeared both as an increase in the rate and as an increase in its depth; for the adapted animals, the rate of the respiration cycles, on the average, increased by 32%, and for the control animals, by 40% (Fig. 6). Even during an acceleration of 20 units, as a rule, there was still difficulty in the respiration movements (expressed in a sharp increase of their amplitude and a significant decrease in the rate), in both the control and experimental animals. After termination of the rotation, there was either smooth and rapid recovery of the respiration (Fig. 6) or compensatory dyspnea (Fig. 5).

Therefore, according to the data of the survival rates as well as the results of the physiological reactions, we can consider that adaptation to oxygen deficiency has a favorable effect on the tolerance to accelerations.

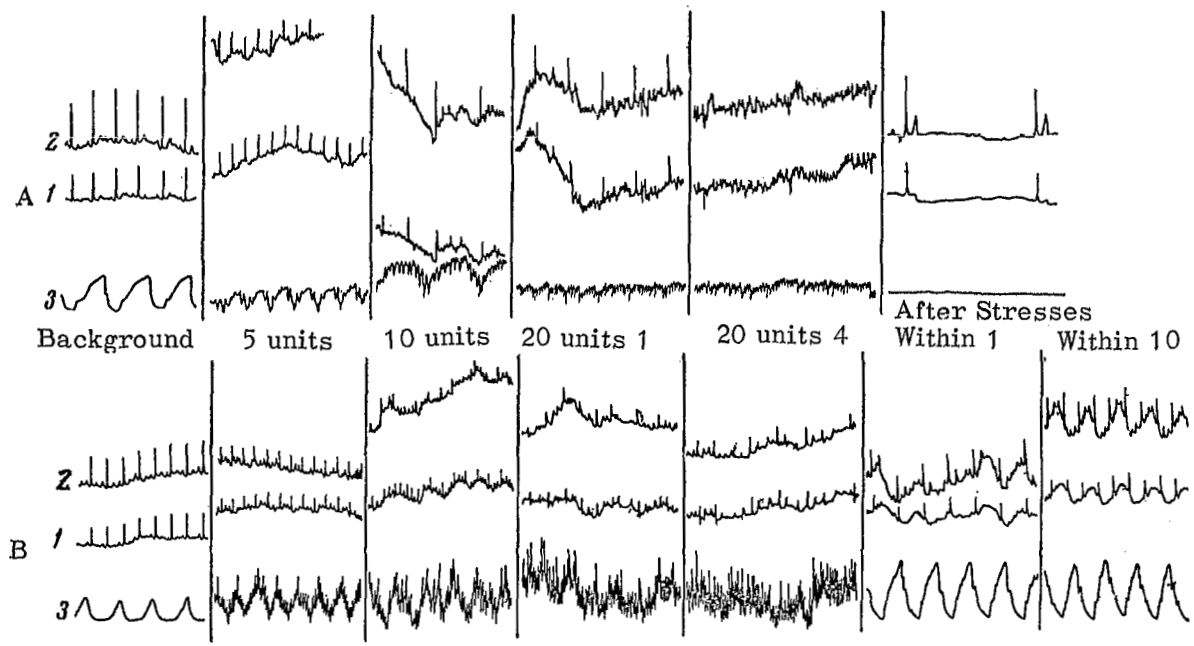

Fig. 5. Electrocardiographs and Respiration in Control (A) and Adapted (B) Guinea Pigs During the Effect of Accelerations. Symbols Same as in Figure 4.

In the experiments on rabbits, we did not find any clear difference in the reactions of the cardiovascular and respirational systems between the adapted and control animals.

TABLE 10. OXYGEN REQUIREMENT FOR THE GUINEA PIGS BEFORE AND AFTER ADAPTATION TO HYPOXIA

Pair No.	Time of Study	Weight of Pair, g	Requirement, ml/15	Requirement, ml in 1 kg/min	M±m	T
1	Before Adaptation, First Day	619	177	19		
2		624	163	16,4	19,8±2,7	
3		652	236	24,1		
1	After Adaptation, First Day	688	140	13,7		
2		710	180	16,9	16,5±1,49	1,0
3		684	193	18,8		
1	Sixth Day	695	165	15,8		
2		725	168	15,4	15,9±0,32	1,5
3		710	173	16,5		

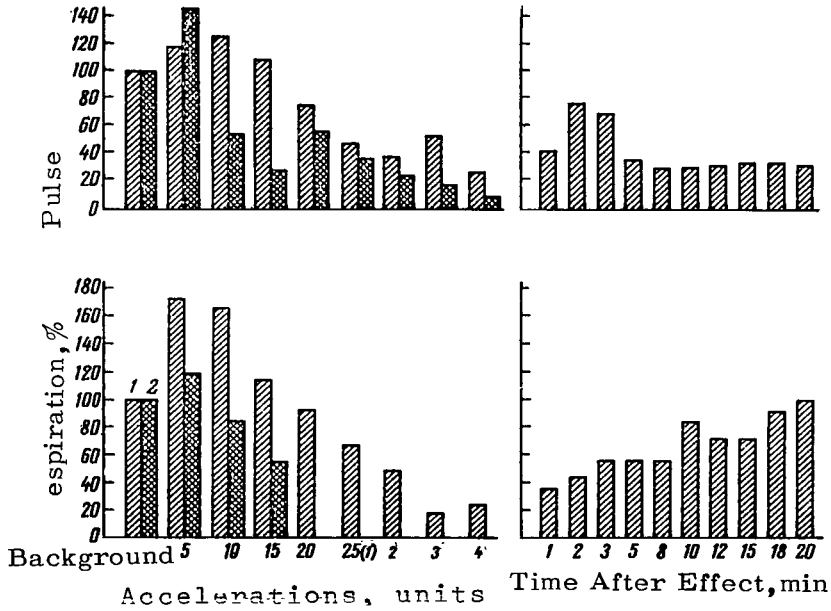

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Fig. 6. Rate of the Pulse and Respiration in Guinea Pigs During the Effect of Accelerations (1) Experiment; (2) Control.

The results of the studies conducted show convincingly that, by means of adaptation to hypoxia, the animals' resistance to the effect of large magnitudes of transversely-directed accelerations

increases significantly. In our experiments, this was expressed both by an increase in the survival rate for the experimental animals and by a lesser degree of disorders in the cardiac activity. The positive effect of the methods used for training was preserved for 2-3 weeks. However, in this case there was a definite relationship between the duration of the adaptation and the general structure of the scheme. If, after a 14-day interrupted adaptation, the survival rate on the third day exceeded that in the control by a factor of three during the effect of an acceleration, then, for a 3.5-day continuous adaptation, there were no differences even on the fourth day afterward. This was substantiated by the less clear and much more rapid transitional changes on the part of the red blood picture.

We did not succeed in establishing a relationship between the effectiveness of the training and the seasonal factors in our experiments. We did not note any essential difference in the resistance to accelerations, which could be related to seasonal features, in the control mice; in the autumn, the survival rate varied from 25 to 50%.

Naturally, a clarification of the type-features of the animals /232 in their adaptation to hypoxia, and the possibilities of developing in them a "condition of non-specifically increaseing resistance" to accelerations [10] by this method, are of great interest. A number of articles, which were published in corresponding collections and monographs, studied the first problem. As for the second, it still has not been studied. Although our experiments, because of the smallness of their number, do not give us the right to answer the latter question, we did obtain certain data, nevertheless, which are of definite interest.

In the fourth series of experiments, we adapted white mice, white rats, guinea pigs, and rabbits simultaneously.

On the basis of the calculations for the survival rates and the changes in the erythrocytes and hemoglobin, we can see that the most significant results were obtained in the experiments on the white mice, and the least significant in the experiments on the rabbits. As for the white rats and the guinea pigs, they occupy an intermediary position; it would be difficult to determine precisely what place they occupy. The low resistance of the adapted rabbits to the effect of the accelerations is not completely understandable. The degree of the reaction on the part of the red blood to hypoxia was roughly the same as for the other types of animals. Therefore, any other mechanisms for adaption were insufficiently effective. It is possible that the weak tonization of the parasympathetic nervous system in this type of animal, to which a number of authors give great significance in relation to their resistance to unfavorable effects of the surrounding medium, is responsible in this case.

The character of the reaction on the part of the red blood, and the results of the study of the oxygen requirement in the adapted animals, conform with data in the literature [1,6,8,12,16, 17].

It is well known that the most general reaction on the part of the heart to the effect of accelerations which are moderate in value is tachycardia, which in individual cases exceeds the original level by 2-3 times. In our experiments, we observed a slight increase in the rate of the heart contractions only in individual experiments. This, probably,can be explained by the fact that placing the animals in a position which is not natural to them caused considerable excitation and the maximum possible increase in the rate of the heart contraction.

If we agree with the concept that the principal pathogenic result of the effect of accelerations is the circulatory and hypoxic type of hypoxia, then the mechanism for the favorable effect of adaptation on the resistance to accelerations becomes completely understandable. However, not all the mechanisms involved in providing an organism with oxygen during adaptation to hypoxia also act during accelerations. We are assuming that during the effect of the accelerations, the respirate may be rapidly disturbed in an identical way for the experimental and the control /233 animals because of purely mechanical compression of the chest. Obviously, the cardiovascular system has a somewhat greater significance. It seems to us, however, that developing polycythemia, rearrangement of the metabolic processes, and physical and chemical factors on the tissue and cellular levels are of particular significance.

In conclusion, we should note that the studies conducted recently by P.V. Vasil'yev and A.R. Kotovskaya on humans have confirmed the experimental observations presented in this article. The resistance of the human subjects to acceleration after adaptation to hypoxia increased by 1.5 to 2.3 units, i.e., roughly by the same amount as the use of an anti-G suit provides.

CONCLUSION

(1) Adaptation to hypoxia is an effective method of increasing animals' resistance to the effect of transversely-directed accelerations. The use of this method, as a rule, increased the survival rate in the experimental groups during the test on on the 1-5th days by 24-46%, in comparison with controls.

The increased resistance to the accelerations was maintained for 10-18 days.

(2) The degree of increase in the resistance is determined by the duration of the adaptation and the general format of the adaptation method.

(3) During intermittent adaptation to a decreased barometric pressure for 14 days, the number of erythrocytes increased by 40% for the mice, by 18% for the rats, by 13% for the guinea pigs, and by 39% for the rabbits; the amount of hemoglobin increased by 39, 15, 7, and 16%, respectively.

(4) The O_2 requirement for the animals at rest before and after adaptation to hypoxia, determined at normal barometric pressure, does not change substantially.

(5) A disorder in the cardiac activity and the respiration is developed sooner, and reaches a greater intensity, for the control animals than for the adapted ones.

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CHANGE IN THE RESISTANCE OF AN ORGANISM TO ACCELERATIONS AFTER THE PROLONGED EFFECT OF SMALL CONCENTRATIONS OF CARBON DIOXIDE

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ABSTRACT: Placing rabbits in an atmosphere with 3-5% carbon dioxide involves a period of prolonged aftereffects which are characterized by changes in the respiration, cardiovascular activity, and bioelectric potentials of the brain, and by a decrease in the body temperature, as well as leukocytosis. During this period, the animals' resistance to the effect of accelerations in a transverse direction, with values from 4.5 to 7 units, is found to be significantly lowered. The change in the animal's reaction when it is affected by small concentrations of carbon dioxide is accompanied by a sharp suppression of the bioelectric activity of the brain; changes in the electrocardiogram indicate a disorder in the excitation behavior as manifested by pareses and paralyses of the posterior extremities. The physiological mechanisms for the decrease in the animals' resistance in relation to violent factors require further studies.

At the present time, in relation to articles studying the problem of habitation in crowded buildings, the attention of researchers has been drawn to the effect produced in an organism by small concentrations of carbon dioxide acting for a long period of time. A determination of those limits for carbon dioxide concentration which do not have a toxic effect on the organism, and which do not change its working capacity, is found to be very important. /234

The data in the literature show that the effect of remaining for a long time in an altered gaseous medium which contains increased concentrations of carbon dioxide can substantially change the organism's reaction to the effect of a different type of extremal factor (high temperature, oxygen deficiency, accelerations, etc.) [1, 2, 4, 5, 8, 10-17, 19]. /235

The purpose of our study was to test this concept on the basis of experiments with animals, which were kept under the conditions of a gaseous medium with an increased percentage of carbon dioxide, and subjected to such violent factors as acceleration.

METHODS

The experiments were conducted on 21 rabbits. Before putting them in an unchanged gaseous medium, the animals were subjected to the effect of an acceleration. The value of the acceleration varied from 4.5 to 7 units, the time for the maximum effect was 60 sec, and the rate of increase was equal to 0.65-0.7 units/sec, while the rate of decrease was 1.3-1.5 units/sec. The animals were put in an aluminum container designed according to the shape of the animal's body, leaving only the head free to move. The acceleration had the direction "back-chest". The rates of respiration and heart contractions, as well as electrocardiograms using the second standard lead were recorded in the rabbits before, during, and after the rotation. Before and after the effect of the acceleration, we recorded the rabbits' electroencephalograms, with a lead on the motor zone of the cortex according to the Sakhiulina method. We observed the character of the recovery of the functions being studied for 15 min after the acceleration. Then the rabbit was put in a chamber with an increased content of carbon dioxide (from 3 to 5%). The time the animals remained in the chamber was 5, 10, 24, 49, 96, 120, and 240 hours. Before they were put in the chamber, and after they were removed from it, we measured their rectal temperature and took blood from their ears in order to determine the percentage of hemoglobin and the quantity of leukocytes. Fifteen minutes after removing them from the chamber, we again subjected the rabbits to the effect of an acceleration with the same characteristic. For the control, we used a group of rabbits which had been subjected only to the effect of an increased percentage of carbon dioxide.

RESULTS

The acceleration caused a decrease in the rate of the respiration and the heart contractions in the rabbits. The rate of respiration during the maximum effect was about 60-80% of the original in most cases; the pulse rate was also about 60-80% of its original value. The pulse returned to its original level within 3-5 min after the acceleration. During the maximum effect, we

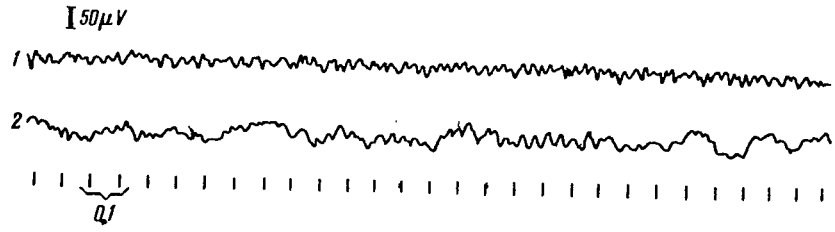

Fig. 1. Electroencephalogram of a Rabbit after Exposure to an Atmosphere with a 5%-Content of CO_2 for 5 Hours. (1) Background; (2) Fifteen Minutes after the Effect.

could note a compression of the *P* and *T* waves on the electrocardiograms, and a decrease in their voltage, as well as a decrease in the voltage of the *R* wave. Toward the end of the maximum effect /236
of an acceleration (in 40 sec.), a pronounced bradycardia frequently changed into a sino-auricular block.

On the electroencephalogram, which was recorded 15 sec after stopping the centrifuge, we observed a disappearance of the α-waves, as well as intensification of the frequency and amplitude of the β- oscillations. The reactivity of the cortex to the transmission of a sound stimulus was lacking for 3-5 min. Normalization of the electroencephalogram occurred within 2-5 min.

The period following the one in which the rabbits were given additional carbon dioxide was characterized by a sharp suppression of the motor activity. The duration for the aftereffects was in direct proportion to the time the animals remained in the chamber. The immobility of the rabbits seemed even more striking, because they hopped, washed themselves, and ate grass while in the chamber. After the effect, we also noted a decrease in the body temperature (by 0.4-1.5°) and an increase in the quantity of leukocytes (by 2000 and 3000). The reaction to sound was either decreased or sharply inhibited. The electrocardiogram was characterized by a predominance of slow high-voltage potentials (Fig. 1).

During the effect of an acceleration after the animal was left in the chamber with the increased percentage of CO_2, the changes in the functions of the respirational and cardiovascular systems, although they had the same direction as in the original condition, were nevertheless much more sharply pronounced (Table 1). We can see from the table that during the effect of an acceleration after the animals were left under the conditions of an altered gaseous medium, there was a sharper retardation of the rate of respiration and heart contractions than during the effect of the same acceleration when the animals were under the conditions of a usual atmosphere. Statistically, these data had a high degree of reliability.

The rate of the respiration for the rabbits was very variable in its original condition. However, during the effect of an acceleration under regular conditions, and particularly after remaining in an atmosphere with an increased content of carbon dioxide, the individual variability decreased by 2.5 times during /237
the general retardation of the rate of respiration. On the other hand, the individual variability of the rate of heart contractions increased somewhat, but serious changes in the muscles of the heart were detected on the electrocardiograms.

The changes in the rate of the respiration and the pulse during the effect of an acceleration on the animals which had been removed from the chamber with the increased percentage of CO_2 were sharper and more prolonged than in the original condition.

TABLE 1: RATE OF RESPIRATION AND OF HEART CONTRACTIONS IN RABBITS DURING THE EFFECT OF AN ACCELERATION, BEFORE AND AFTER A STAY IN A CHAMBER WITH AN INCREASED PERCENTAGE OF CARBON DIOXIDE.

Group of Animals	Number of Experiments, n	Freq. of Resp, min				Freq. of Heart Contractions, beats/min			
		$\bar{x} \pm \sigma$	m	t_1-2	t_1-3	$\bar{x} \pm \sigma$	m	t_1-2	t_1-3
Control	21	138±61	13,3	—	—	240±33	7,17	—	—
During the Effect of an Acceleration	20	103±46,6	10,4	2,07	—	145±46	10,2	7,6	—
During an Acceleration, After the Effect of the CO_2	21	82±29,5	6,4	—	3,8	140±58	12,6	—	6,8

This was particularly clearly apparent in the experiments when the animals were kept in the chamber for a relatively short period of time (up to 96 hours).

Thus, for example, in Experiment No. 9 the rate of the respiration during the maximum effect of an acceleration, before the chamber experiment, was 70% of the original, and only 38% after the chamber experiment; the pulse rate changed from 86 (before the chamber) to 25% (after the chamber), respectively.

On the electrocardiograms, even within 25-30 sec of the maximum acceleration, there were signs of a sino-auricular block which lasted longer than during the rotation in the original condition.

After the acceleration, there was mild exophthalmus in the rabbits.

On the electroencephalograms, there was a sharp suppression of the bioelectric activity of the brain. This was expressed in an almost complete flattening of the encephlographic curve. Only rarely could we note the appearance of slow oscillations. The flat character of the electroencephalogram was frequently preserved for 30-45 min. All this time, the animals sat completely immobile, and did not react to sound stimuli. The EEG then gradually returned to normal (Fig. 2).

The effect of the acceleration also caused more remote aftereffects. In one of the experiments, a rabbit which was kept in an atmosphere with 4.5-5% CO_2 for 5 hours and then subjected to the effect of an acceleration of 5.8 units was found dead after 10 hours. During the autopsy, we found that its heart was considerably enlarged and completely filled with blood. Beneath the pericardium /238 along the length-wise axis, there was a rupture of the heart muscle.

In another experiment, for a rabbit which was left in a chamber

with a 3%-content of CO_2 for 48 hours and then subjected to the effect of an acceleration, a paresis of the posterior extremities developed during the following days. The boundary for the loss in pain sensitivity was observed in the region of the pelvic girdle. During the following days, there was observed a brief appearance of pain sensitivity, beginning on the left hip, and then on the right. The pain sensitivity in the region of the pelvic girdle was found to be more intensified. The rabbit died on the eleventh day.

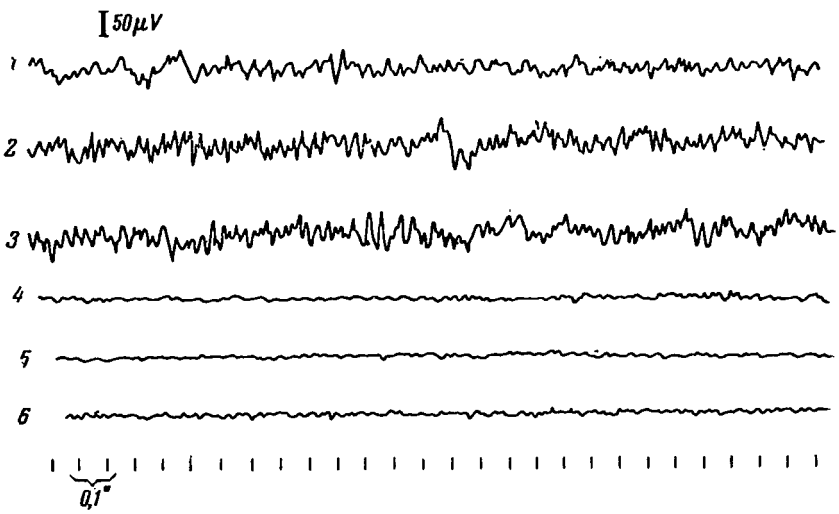

Fig. 2. Electroencephalogram of a Rabbit after the Effect of Acceleration and of Remaining in a Chamber with a 3%-Content of CO_2 for 24 Hours. (1) Background; (2) Fifteen Seconds After an Acceleration of 6 units; (3) Fifteen Minutes After the Effect of CO_2; (4) Fifteen Seconds After the Effect of an Acceleration of 6 units; (5) Five Minutes After the Effect of Acceleration; (6) Ten Minutes After Acceleration.

A histological analysis showed the presence of changes in the lumbosacral section of the spinal cord.[1] In the dorsal half of the fifth lumbar segment, there was a focus of malacia encompassing the white and gray matter. The anterior spinal crescents contained very few nerve cells. A large number of motor neurons were irrevocably changed (all the way to "cell-shadows"). In the space between the sixth and seventh lumbar segments, we found only single non-recoverable forms in the anterior spinal crescents. In the more caudal leads, the picture became completely normal. The spinal ganglia were within the limits of the norm. /239

[1]All the histological data were obtained and kindly placed at the disposal of the authors by Professor V.P. Kurkovskiy, Director of the Neurohistological Laboratory at the Neurosurgical Institute imeni Polenov.

We should emphasize the fact that there were no injuries observed in the skeletal structure of this animal. The nature of the histological changes indicated that the cause was a breakdown in the supply to the nerve cells as a result of the effect of an acceleration on the animal. It is still difficult now to speak about the mechanisms of this phenomenon. However, we should say that the picture of the changes differed from that which we had during the effect of accelerations in the longitudinal direction on an animal [7]. However, both for those and for the other accelerations, the location for the changes in the nerve cells was the lumbosacral section.

In one of the rabbits, after it had been in a medium with a 5%-content of CO_2 for 5 hours, there were changes in the electrocardiogram during accelerations which showed serious disorders on the part of the myocardium: an increase in the *Q* wave and the appearance of a negative *T* wave. These changes were maintained for 3 days. They could be either the result of the appearance of a myocardial infarction or the result of a sharp turning of the heart.

In still another rabbit, there was an incomplete, brief paresis of the posterior extremities after it was kept in an atmosphere with a 3%-content of CO_2 for 48 hours, and after an acceleration.

It is important to note that all these disadvantageous occurrences in the experimental animals after the accelerations were noted after they were kept under the conditions of an altered gaseous medium for a relatively short period of time: from 5 to 48-96 hours. When they were kept in the altered gaseous medium for a longer period of time, the subsequent acceleration affected the change in the functions of the respiration and the blood circulation less sharply.

DISCUSSION OF THE DATA OBTAINED

A comparison of the data concerning the condition of the functions being studied during the effect of an acceleration, before and after being put in an altered gaseous medium, shows that they change more sharply in the latter case. The suppression of the bioelectric activity in the brain, the more pronounced changes in the rate of respiration and of the heart contractions (during an increase in velocity, at the maximum acceleration, and after stopping the centrifuge), the changes in the electrocardiograms, and, finally, the rupture of the cardiac muscles - all of this together indicates that small concentrations of carbon dioxide can cause substantial changes in the animal's reactivity in relation to considerable stresses.

It is still too soon to speak about the essence of the physiological mechanisms causing the change in the animal's reactivity when affected by small concentrations of carbon dioxide. Obviously, the suppression of the functional condition of the higher parts of /240

the central nervous system, as well as the decrease in the circulatory reserves as a result of the changes in the cardiovascular system and the suppression of the hormone activity and the activity of the oxidizing enzyme systems, play an important part here [9, 18]. But the very fact of the presence of this changed reactivity, accompanied by such serious phenomena as paralyses or ruptures of the cardiac muscles, shows the necessity for a detailed study of the immediate and later aftereffects for every excess in the composition of a gaseous medium, even in those cases when this excess is realized during normalization.

The experiments show that each excess is tolerated somewhat easier if it occurs after a more prolonged period in changed gaseous media. Obviously, in those cases when the animal has become more adapted to these conditions, when there is some relative stabilization in the function of all of its organs and systems (caused by this adaptation), the transition to new conditions for a gaseous medium occurs more easily. In those cases when this transition occurs during the beginning period of adaptation, during the period of intensified activity for all the physiological mechanisms, each new stimulus such as the acceleration in our experiments) can prove to be extreme. That is why the changes in the animals' reactivity after they were placed in the chamber for 48-96 hours were much sharper than after they were kept under the altered conditions of a gaseous medium for 120-240 hours.

CONCLUSIONS

Keeping the rabbits in a gaseous medium with an increased content of carbon dioxide for a long period decreases their resistance to the effect of accelerations in a transverse direction.

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CHANGE IN OXYGEN CONTENT IN BRAIN TISSUE DURING THE EFFECT OF ACCELERATIONS IN VARYING DIRECTIONS

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ABSTRACT: The oxygen pressure in the tissues of the cerebrum was studied in cats and rabbits during the effect of accelerations. It was established that the change of the pO_2 in the brain tissue depends on the value as well as the vector of the stress. The greatest decrease in the pO_2 is observed for the direction "pelvis-head" for 5-7 units, which corresponds to a climb to an altitude of 9-10,000 meters. For the same values of the effect in the direction "head-pelvis", the changes correspond to those which take place at a climb of 3-5,000 meters.

Although many authors [1, 3, 13, 14, 16, 36] link the development of disorders in the activity of the central nervous system during accelerations with the phenomena of oxygen deficiency, the problem itself (concerning the condition of the oxygen supply to the brain under these conditions) nevertheless has still been insufficiently examined. The attempts of individual researchers [9, 13, 23, 36] to evaluate the condition of the cerebral circulation during accelerations solely on the basis of the arterial pressure in the vessels which feed the cerebrum can not be recognized as physiologically substantiated. As shown by many researchers [4, 5, 8, 20, 21, 24, 29, 31-35], there is no strict correlation between the value of the arterial pressure and the condition of the cerebral circulation. Thus, according to certain data, the blood circulation in the vessels of the brain is not substantially weakened even during a decrease in the arterial pressure to 30 mm Hg [20]. /241

Even more complex interrelationships between the arterial pressure and the cerebral circulation can take place during accelerations especially during the effect of accelerations in the direction "head-pelvis", when there are sharp changes in the pressure in the venous vessels in addition to a change in the pressure in the arterial part of the vascular system. The appearance of a negative pressure in the veins brings about preservation of the gradient of the arteriovenous pressure [10, 26, 27]. The blood circulation in the cerebral vessels can be preserved in this case, even when the arterial pressure decreases to extremely small values [10, 15, 28, 30]. The lumen of the venous vessels during the appearance of very significant negative pressures in them remains /242

patent because of their distribution in the isolated cavity of the cranium, in which a negative pressure of the liquid is produced during this time.

Therefore, a number of purely physical phenomena can favor preservation of the cerebral blood flow even during very rapid changes in the total hemodynamic picture.

A clarification of the problem concerning the degree of hypoxia to which the central nervous system is subjected during the effect of accelerations would undoubtedly aid in determining the oxygen content directly in the brain tissue. This possibility was discovered through the development of the polarographic method for determining the concentration of oxygen in the tissues with the aid of solid electrodes made of platinum [11, 22]. Although the first studies using this method were conducted in 1956 [25], the number of studies accomplished in this direction is nevertheless still insignificant.

Thus, in experiments on anesthetized cats, it was established [25] that the effect of accelerations in the direction "head-pelvis" for average values, causes a substantial decrease in the oxygen pressure in the surface layers of the brain. Somewhat different results were obtained in chronic experiments on dogs [7]. These studies established the fact that the pO_2 in the brain tissues decreases only during accelerations with values greater than 4 units. For lesser values of the stresses, the oxygen content in the cerebral tissues increases somewhat during the momenty of the effect. According to the data of the authors, the most pronounced changes in the pO_2 in the brain tissue are observed during accelerations in the direction "head-pelvis". However, we should note that the data presented on the oxygen pressure in the brain tissue have only an approximate nature, since a quantitative determination of the pO_2 by using electrodes of the open type is highly relative. In view of this, the results of the studies are not sufficiently accurate for determining the degree of hypoxia to which the central nervous system is subjected during the effect of an acceleration. Meanwhile, this problem is of great interest from both the theoretical and practical standpoints. This study also includes an examination of this problem.

The tests were conducted on unanesthetized animals (cats and rabbits) in chronic experiments. The oxygen pressure was determined polarographically according to the value of the diffusion current with a potential difference of 0.65 V [12, 22]. For the cathodes, we used stationary platinum electrodes with diameters of 0.14 mm, inserted 5-7 days before the beginning of the experiment into various sections of the cerebrum with the aid of a stereotaxic apparatus. For the anode, we used a silver-chloride electrode with an area of 4 cm^2, attached with the aid of a clamp to the internal surface of the concha auriculae, which was first smeared with electrode paste. In order to record the diffusion

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currents, we used a micrograph (Type BD-I, made by the "Kippa" firm).

The accelerations were reproduced in a centrifuge with a radius of 2 m. Particular attention was given to fixing the animals on the test-stand. In order to reduce the local accelerations to a minimum, we put the animals in special containers whose shape corresponded to the configuration of their bodies. For a more uniform distribution of the stress over the surface of the body, the inside walls of the container were padded with a layer of foam plastic.

We examined the effect of accelerations in two directions: "head-pelvis" and "pelvis-head". The cats were subjected to accelerations with values from 2 to 23 units in the direction "head-pelvis", and from 2 to 10 units in the direction "pelvis-head". In the experiments on rabbits, the value for the accelerations varied from 2 to 12 units ("head-pelvis") and from 2 to 5 units ("pelvis-head"), respectively. In most cases, the time for the effects lasted from 30 sec to 1 min.

In conducting the experiments, we decided not to evaluate the polarograms by the so-called oxygen tests [6, 12], since the reaction of the cerebral vessels to hyperoxia was not always uniform. We decided to use a different method for this purpose; we called it the method of "altitude tests". The latter included obtaining the polarograms which corresponded to a certain degree of hypoxia: the animals were subjected to a "climb" to a given altitude in a pressure chamber. In this case, the recorded polarograms were compared with the following ones, which were recorded in the animals during the effect of accelerations. The data from the "altitude tests" were also used for constructing calibration graphs.

In order to conduct the altitude tests, we used a pressure chamber with a volume of 0.2 m^3. The "climb" to the altitude and the "landing" from the altitude were realized at an average velocity of 50 m/sec. The time the animals remained at altitudes of 6 km (cats) and 5 km (rabbits) varied from 1.5 to 3 min in most cases; at an altitude of 10 km, it was no longer than 1 min. In order to eliminate the effect of one factor on another (oxygen deficiency on acceleration, or vice versa), the "climb" to the altitude preceded the effect of the accelerations in some experiments, while the "climb" came after the stresses in the other experiments. In several experiments (controls), the "climb" of the animals to an altitude of 5 km was made both before and after the rotation in the centrifuge. /244

In order to determine the animals' tolerance to acceleration, we recorded the respiration, electrocardiogram, and (in some cases) the electroencephalogram. We performed 37 experiments on 4 cats and 11 rabbits. In each experiment, the animals were subjected to the effect of 3-10 accelerations.

The examinations conducted showed that the oxygen content in the brain tissue changes in various ways in relation to the value, direction, and recurrence of the effect of the acceleration. /245
During accelerations of 1.5 - 3.5 units in the direction "head-pelvis", for example, the oxygen pressure in the brain tissue at the very moment of the acceleration usually increased somewhat or remained at the original level (Fig. 1). During accelerations of greater values (5 to 7 units for the cats, 4.5 to 5.5 units for the rabbits), it also increased somewhat at the beginning of the effect, but then, within 15-30 sec, it decreased either to the original value or even somewhat lower; however, it remained within the limits of variation for the physiological norm. During accelerations of 8-12 units for the cats and 6-9 units for the rabbits, the oxygen pressure decreased substantially, both in the cortex and in the subcortical structures (Fig. 1). This decrease became greater when the value and the duration of the extreme stress increased. Nevertheless, we did not observe any strict relationship between the value of the acceleration and the oxygen pressure in the brain tissue. A comparison with the results of the "altitude tests" showed that the oxygen pressure in the brain tissues was

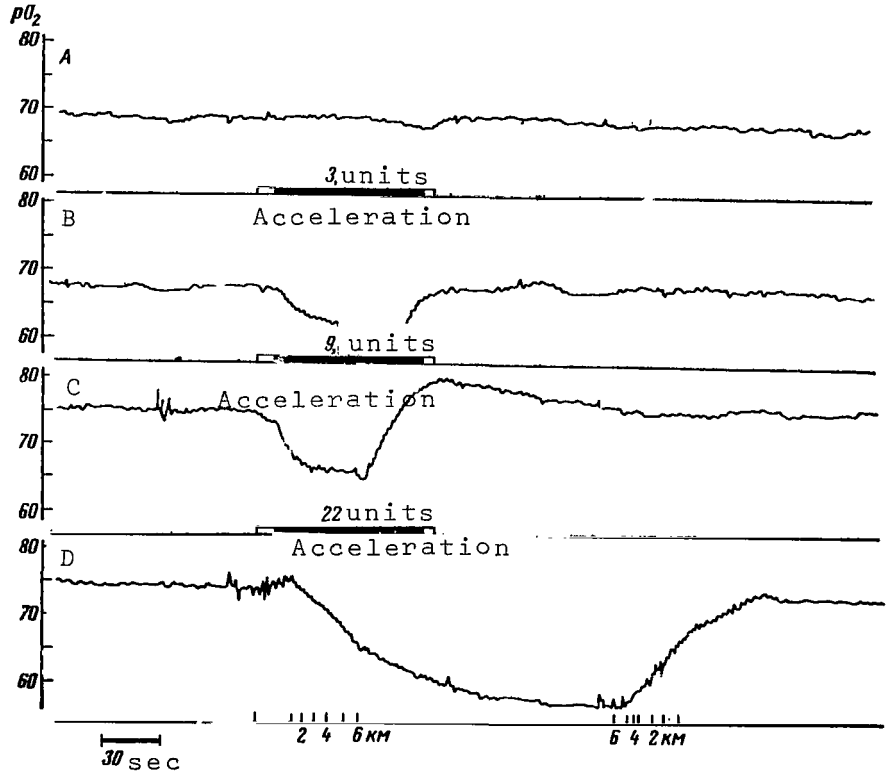

Fig. 1. Oxygen Pressure in the Brain Tissue of a Cat for Varying Values of Acceleration. (A), (B), and (C): During the Effect of Acceleration; (D): During the "Altitude Test"

higher in this case than during the climb to an altitude of 5000 m (Fig. 1D).

The pO_2 in the brain tissue changed in a completely different manner during the effect of accelerations in the direction "pelvis-head". In this case, even rather small stresses were accompanied by a very steep decrease in the oxygen pressure (Fig. 2). In contrast to the accelerations in the direction "head-pelvis", the oxygen pressure during the accelerations in this direction dropped almost vertically. A comparison with the data from the "altitude tests" showed that the oxygen pressure in the brain tissue decreased in this case to a level which corresponds to an altitude of 8-10,000 meters (Fig. 2D). Substantial differences were also observed in the recovery rate of the pO_2 after the termination of the accelerations. While the recovery of the pO_2 in the brain tissue usually began immediately after termination of the stresses, and had a smooth curve for accelerations in the direction "head-pelvis" (average values), after accelerations in the direction "pelvis-head" it occurred much later. In relation to the value of the stress, there were observed two variations of returns

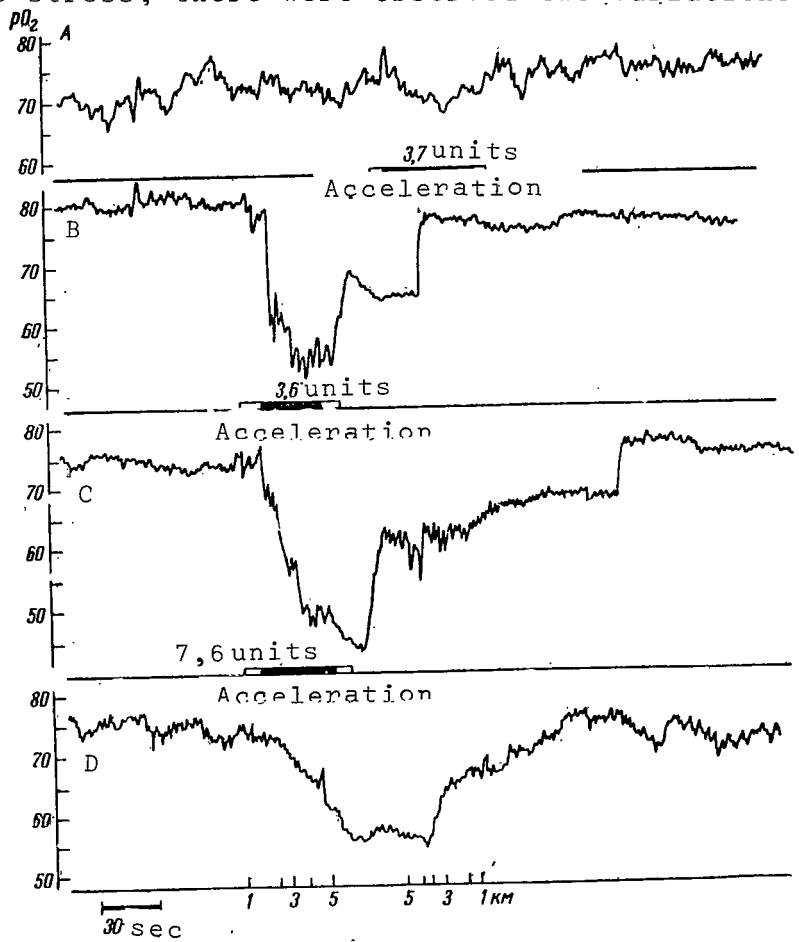

Fig. 2. Oxygen Pressure in the Brain Tissue of a Rabbit, in Relation to the Direction of the Acceleration (A): During Acceleration in the Direction "Head-Pelvis"; (B) and (C): Same, "Pelvis-Head"; (D): During an "Altitude Test"

to the original pO_2 level. After accelerations of small values, the recovery of the pO_2 had a step wise character (Fig. 2 B,C). After the effect of accelerations which were close in value to the tolerable maximum or after the repeated effect of accelerations with average values, the return of the pO_2 to its original level occurred only after a phase showing a significant increase /246
in the oxygen pressure. It is interesting to note that the animal continued to remain in a state of sharp inhibition during this period and did not react to imposed stimuli. In those experiments where we recorded the animal's electroencephalogram, we observed in the latter a sharp suppression of the bioelectric activity, with a predominance of the slow waves. The external respiration and the activity of the cardiovascular system during this period were very /247
to the original. Immediately after the end of the phase with the increase in the pO_2, the animal began to react to the stimuli, while there were found more frequent rhythms on the electroencephalograms. Obviously, the cause for the significant increase in the oxygen pressure during the immediate aftereffects for the acceleration is the decrease in the oxygen requirement for the nerve tissue.

We should note that similar phenomena, but less pronounced ones, were also observed during accelerations in the direction "head-pelvis" in the case when they were close to the tolerable maximum in value.

It follows from the above that the change in pO_2 in the brain tissue is definitely related both to the value and to the vector of the acceleration. The oxygen pressure decreases most sharply during accelerations in the direction "pelvis-head". During accelerations of 5 - 7 units in this direction, the hypoxia to which the central nervous system is subjected corresponds to that which is observed during a climb to an altitude of 9-10,000 meters. For stresses of the same value, but in the direction "head-pelvis", the changes in the oxygen pressure in the brain tissue do not exceed the limits for those which occur during a climb to an altitude of 3-5,000 meters. For stresses of lesser value in this direction (up to 5 units), the oxygen pressure in the brain tissue remains at a level which is close to the original.

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MORPHOLOGICAL AND CERTAIN HISTOCHEMICAL CHANGES IN THE PRECORONARY REGION OF THE CEREBRAL CORTEX IN DOGS DURING THE EFFECT OF TRANSVERSE ACCELERATIONS

D.I. Medvedev

ABSTRACT: The morphological changes in the precoronary region of the cerebral cortex in male dogs were examined for the effect of the following accelerations: 8 units for 3 minutes and 12 units for 1 minute. There were some small hemorrhages, and occasional vacuolization of the cytoplasm and chromotolysis of the nerve cells. Changes in the quantity of ribonucleic acid in the cytoplasm and nucleus of the nerve cells are also described. These changes have a reversible nature.

There are only a few articles in the available literature on the study of the effect of accelerations on the nerve tissue. /248

Thus, A.M. Razumeyev and P.N. Suvorov [7], having studied the dynamics of the changes in the bioelectric activity of the cerebral cortex during the effect of transverse accelerations, found the appearance of rapid β-waves, which quickly change into an α-rhythm and then into Δ-waves, in the cerebral cortex at the beginning of the effect. In experiments on rabbits, there is an almost complete disappearance of the bioelectric activity in the cerebral cortex during the effect of an acceleration of 7 units for 10 minutes. After termination of the effects in the centrifuge, the bioelectric /249 activity of the cerebral cortex recovered rapidly.

The data of Yu.Ye. Moskalenko, O.G. Gazenko, et al. [6] on the study of the blood supply to the cerebrum during the conditions of acceleration show that the adaptation reactions of the vascular system in the brain play an important part in the appearance of resistance of the cortex to this effect.

Moreover, in a study by N.N. Zhukov-Verezhnikov, V.I. Yazdovskiy, et al. [4], it is shown that the "tolerance of animals and men to flight is linked not only to the perfection of the organism's compensatory systems, but also to the significant stability for a living cell in relation to the preliminary effects of a flight".

A morphohistochemical examination of the labyrinth in animals subjected to accelerations, conducted by Ya.A. Vinnikov and his coauthors [3], showed that, immediately after the accelerations, there is a severe impoverishment of ribonucleic acid in the proto-

plasm of the hair cells in the utricular spot, and a displacement of the nucleus in the direction of the acceleration vector, as well as a contraction of the nuclei of the hair cells. The recovery process lasted 4 hours and longer.

In a study by I.M. Khazen [8], it was noted that "during a histological examination of the cerebrum in rats which had been subjected to the effect of acceleration, there was found a clear amitotic separation of the nerve cells".

In this study, we examined the changes in the pre-coronary region of the cerebral cortex in adult male dogs during the effect of accelerations with values of 8 units for 3 minutes (Series I of the experiments), and with values of 12 units for 1 minute (Series II of the experiments). On the basis of studies by the I.P. Pavlov school, we examined this region in the dogs as a nuclear zone of a motor analyzer.

The nucleus of the motor analyzer is located in the sigmoid gyrus where the fields PrC_1 and PrC_2 are found [1]. These field are characterized by a narrow cortex, by a lack of a fourth layer and the presence in the fifth layer of a large number of gigantic pyramidal Betz cells, and also by a comparatively wide third layer.

The dogs were killed by ether vapor within 1 hour and 1, 3, 7, 15, 30, and 60 days after the effect of the accelerations. In both Series I and Series II of the experiments, we examined two dogs in each period. We examined 28 experimental animals and 2 controls.

The materials were fixed in 10%-formalin, in 96°-alcohol, and in Carnot liquid, and mounted in paraffin and celloidin. In the study, we used the following methods: hematoxylin-eosin, staining with thionine (Nissl), staining with Sudan III for fat (frozen sections), detection of ribonucleic acid according to Brash, and staining with Schiff reagent and periodic acid (Schick reaction). The thickness of the paraffin sections was 5-7μ and that of the celloidin was 10-12μ.

The macroscopic changes after the accelerations were expressed in hyperemia in the pia mater and the surface vessels of the brain. /250

In examining the preparations stained by hematoxylin-eosin, we should note the edematousness in the cerebral tissues, in the form of significant perivascular and partly percellular swellings.

In many of the dogs, there were small hemorrhages, occurring both as ruptures in the vascular wall and as leakage of erythrocytes per diapedesin. These hemorrhages were located mainly at the boundary of the white and gray matter, and also in the second and third layers of the cortex. They were found most frequently in the

Fig. 1. Normal Ganglionic Nerve Cell in the Fifth Layer of the Cortex. The Nissl Substance, in the Form of Bacilliform Lumps is Oriented Along the Length of the Axis of the Cell. Staining with Thionine According to Nissl. Objective: 90x; Ocular: 15x. /251

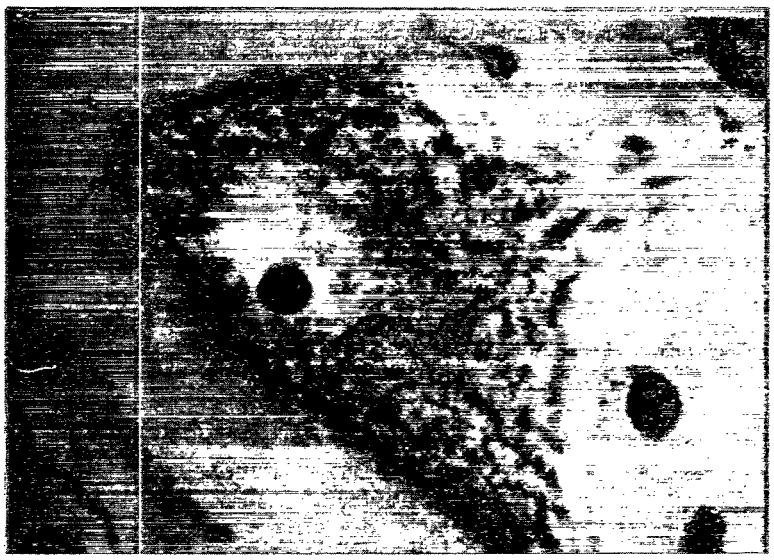

Fig. 2. Ganglionic Nerve Cell in the Fifth Layer of the Cortex on the Seventh Day After Acceleration of 8 units for 3 min. The Nissl Lumps, in the Form of Powdered Granules, are Arranged Concentrically Around the Nucleus. At the Periphery of the Protoplasm, the Formation of an Optically Clear Space has Begun. Staining with Thionine According to Nissl. Objective: 90x; Ocular: 15x.

Fig. 3. First Days After Accelerations of 8 Units for 3 Minutes. /252
Nerve Cell in the Fifth Layer of the Cortex. The Oligodendroglia Cells are being Incorporated in the Protoplasm of the Ganglionic Nerve Cell. Staining with Thionine According to Nissl. Objective: 90x; Ocular: 15x.

Fig. 4. Three Days After Accelerations of 8 Units for 3 Minutes. Withdrawal of the Nucleole from the Nucleus. Nissl Lumps in the Form of Powdered Granules. Ganglionic Nerve Cell in the Fifth Layer of the Cortex. Staining with Thionine According to Nissl. Objective: 90x; Ocular: 15x.

dogs in Series I of the experiments, at times immediately following the experiments (1 hour, 1 day, 3 days). They were found much less frequently during later periods. They were not found at all in many of the dogs in Series II.

In the preparations stained in thionine by the Nissl method, there was observed change (progressive with time) in the location and shape of the Nissl substance in the gigantic pyramidal cells of the fifth layer of the cortex within 1 hour (and after 1, 3, 7, and 15 days) in both Series I and Series II of the experiments. In the control animals, the Nissl substance in these cells is distributed uniformly over the entire body of the cells, mainly in the form of rather large bacilliform lumps extended along the length of the axis of the cells (Fig. 1). After the effect of the accelerations, the Nissl lumps in most of the cells acquire a type of powdered or rounded granules, and are arranged concentrically around the nuclei of the nerve cells (Fig. 2). There is often peripheral chromatolysis. In many of the cells, there are vacuoles around the periphery of the protoplasm. At the same time, the number of cells which show a capacity for being stained intensely with thionine increases. Such nerve cells acquire an elongated shape. The stain is distributed diffusely over the entire perinuclear protoplasm. As a result, the Nissl lumps become almost uniform. The cell nucleus, which is usually light under normal conditions, is also stained diffusely by thionine. The periphery of the protoplasm in such hyperchromic cells is often free from dye and is optically clear. At the same time, there is sometimes an increase in the activity of the oligodendroglia, whose cells are inserted in the protoplasm of the nerve cells in a number of cases (Fig. 3).

The nucleoles were stained intensely during the first days after the effect; in many cases, they moved toward the periphery of the nuclei. There was often a complete withdrawal of the nucleole from the nucleus (Fig. 4). Such phenomena were found very infrequently in the control animals. The direction of the withdrawal of the nucleoles from the nuclei is not strictly limited, and does not depend on the direction of the accelerations.

In the third layer of the cortex, during the first two weeks after the effect of the accelerations, there is also an increase in the number of hyperchromic cells. In the nerve cells of the second and sixth layers of the cortex, there is an initial chromatolysis and vacuolization of the protoplasm in the cells (Fig. 5). /253
During later periods after the experiment (15, 30, and, in part, 60 days), the number of binucleolar and binuclear cells increases. Sometimes we can also observe constriction of the nuclei. Obviously, these pictures of amitotic fission show a compensatory reaction of the nerve tissue.

The phenomena described disappear in most cases around the 30th day, especially around the 60th day, and the morphological

picture of the precoronary zone in the cortex differs little from the norm during this time.

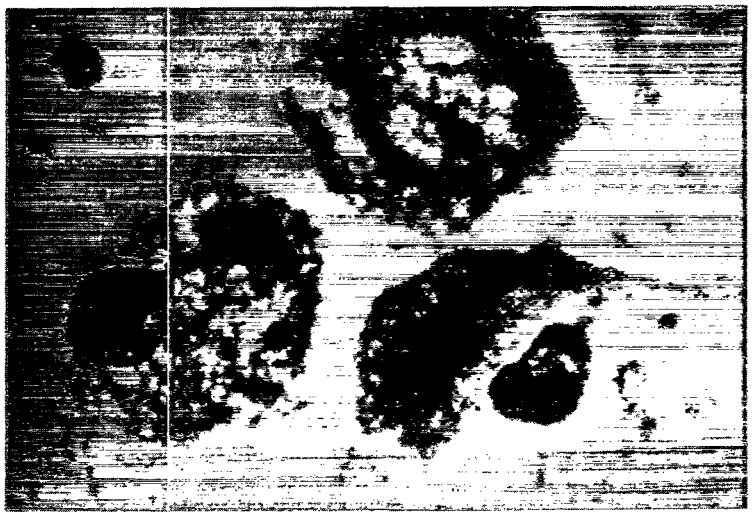

Fig. 5. First Day After Accelerations of 8 Units for 3 Minutes. Nerve Cells in the Second Layer of the Cortex. Peripheral Chromatolysis, Activation of the Oligodendroglia. Staining with Thionine According to Nissl. Objective: 90x; Ocular: 20x.

The fat cells, detected during staining of the frozen sections with Sudan III, were found in the form of numerous clusters around the vessels. The quantity of this perivascular fat varied greatly in different dogs. Moreover, for 2 dogs in the second series of experiments, there were a number of Betz ganglionic cells in the fifth layer of the cortex within 7 and 30 days. During later periods, we were unable to find any fat in the nerve cells. It is very probable that the appearance of fatty inclusions in the cytoplasm of the nerve cells is linked to the age of the dogs, and not to the effect of the accelerations.

During the first day after the experiment, there is a definite increase in the quantity of ribonucleic acid in both series. The quantity of ribonucleic acid increases very rapidly within 1 hour after rotation in the centrifuge. On about the third day, the quantity of ribonucleic acid decreases to the norm. On the seventh /254 and fifteenth days, there is another increase in the ribonucleic acid content. After 3 more days, the percentage of ribonucleic acid is normal and remains close to the norm for 60 days after the experiment.

It is well known that the amount of ribonucleic acid differs in relation to the functional state of the cell, and is closely linked with the synthesis of protein in the latter. During adequate stimulation of the nerve system, there is an increase in the amount

of ribonucleic acid in the cytoplasm of the nerve cells [2].

In relation to this, we can assume that the described increase in the ribonucleic acid during the first day after the acceleration is caused by the functional tension of the nerve cells, and perhaps is linked with an increase in the synthesis of protein in them.

In processing the sections with the Schiff reagent with periodic acid, there was observed in a number of dogs a Schick-positive staining of the protoplasm in the Betz ganglionic cells, in the region where the processes were removed (most often in the region of the axon monticulus). This stain is a type of diffuse pink area which takes up a large part of the protoplasm in the cells. In the region of the Schick-positive staining, the Nissl substance is not found. When stained with thionine, this region acquires an intensely blue color, while all the other structures are stained by thionine to a violet color. The Schick-positive staining of the protoplasm described above was found very clearly in the dogs of Series I of the experiments, and occurred as an immediate after-effect (within 1 hour, and within 3 days after the effect); it was found less clearly in the dogs of Series II of the experiments at later periods (within 30 days after the effect). In order to explain the nature of the phenomenon described, additional histochemical examinations are necessary.

CONCLUSION

The data we obtained show that the effect of accelerations leads to a number of morphological and histochemical changes in the precoronary region of the cerebral cortex.

The nature of these changes in both series of the experiments, and the dynamics for their development, do not coincide basically. However, the time factor is definitely important, and the changes in Series I are more pronounced than in Series II.

We can assume that most of the morphohistochemical changes occurring after the effect of acceleration is linked with the development of inhibiting processes in the cortex. These processes are necessary for the recovery of normal activity in the nerve cells.

This assumption can be based on the fact that the above-described pictures for the change in the location of the Nissl substance, the increase in the quantity of hyperchromic cells, the appearance of an optically clear space at the periphery, etc., largely correspond to the morphological pictures described by B.N. Klosovskiy and Ye.N. Kosmarskaya for carotid inhibition [5]. /255

The changes detected have a transitional nature in the overwhelming majority of cases; as a rule, they disappear within two months after the stress in the centrifuge.

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REACTION AND ADAPTATION OF THE CENTRAL NERVOUS SYSTEM TO STAGNANT ANOXIA (RADIAL ACCELERATION IN ONTOGENESIS)

L. Jílek, S. Trojan, J. Fischer, and L. Krulich

ABSTRACT: The resistance of the central nervous system to hypoxia, which is formed by a positive radial acceleration of a value of 10 g, is examined in rats during early postnatal ontogenesis. Resistance to hypoxia is linked with age. The younger the animal, the fewer the disorders observed in the central nervous system during accelerations. The older the animal, the more differentiated the nerve tissue and the lower the tolerance.

A radial acceleration which exceeds 6 g interrupts the blood circulation and causes complete stagnant anoxia (ischemia) in all the tissues, including the central nervous system; the changes in the latter depend on the ontogenetic maturity of the nerve tissue [3]. In our experiments, stagnant anoxia of the central nervous system was caused by a positive radial acceleration of 10 g in a special centrifuge [8], in rats during their postnatal period. /255

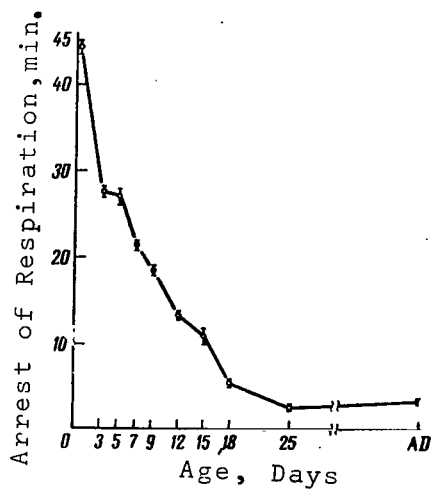

Fig. 1. The Resistivity of the Rats to Stagnant Anoxia Caused by a Positive Radial Acceleration of 10g. AD - Adult Features

RESISTANCE OF THE CENTRAL NERVOUS SYSTEM TO STAGNANT ANOXIA /256

A non-recoverable arrest of the respiration was considered as the criterion for stability.

The greatest stability was observed in newly-born animals (44 min, 15 sec - Fig. 1). It decreased continuously for about 25 days (2 min, 50 sec). For the mature characteristics, the resistivity changed substantially (3 min, 7 sec) [8].

BIOCHEMICAL CHANGES IN THE CENTRAL NERVOUS SYSTEM CAUSED BY STAGNANT ANOXIA

From the biochemical point of view, the following factors have a determinant significance in the reaction of the nerve tissue to stagnant anoxia [7]:

(a) Energy reserves in the central nervous system, particularly those which can be used anaerobically: tissue glycogen, free glucose, and high-energy phosphates.

(b) The intensity and quality of the metabolism in the central nervous system, i.e. the rapidity and manner of using the energy reserves.

(c) The accumulation of catabolites and their fate, i.e., changes in Ph, ion composition, osmotic pressure, etc.

We should keep in mind that the greatest reserves of carbohydrates are contained in the brains of newly-born individuals; they increase rapidly for the first five days of postpartum life, and again increase when the higher divisions of the central nervous system become mature. For the mature individuals, they exceed the level of the newly-born animals (Fig. 2 [3]. Thus, the development of resistivity is not parallel to the development of carbohydrate reserves. /258

According to its intensity, the exchange can be classified as the following: a functional exchange, which provides the energy for the functioning of unharmed (intact) nerve tissue under physiological conditions; an exchange during complete rest, which does not perform special functions, but which is characterized by an

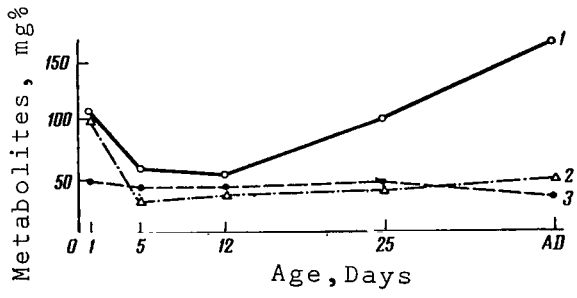

Fig. 2. Percentage of Glycogen, Free Glucose, and Lactic Acid in the Rat Brain during the Postnatal Period (1) Glycogen; (2) Glucose; (3) Lactic Acid

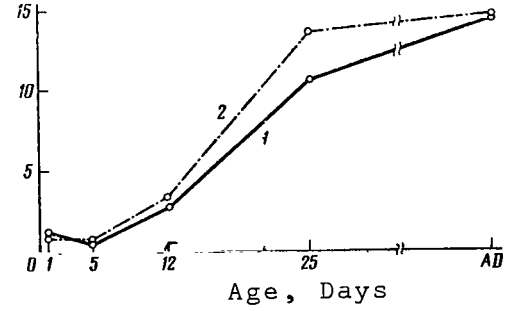

Fig. 3. Absorption of Glycides (1) and Formation of Lactic Acid (2) in the Brain during Stagnant Anoxia. (Calculation for 1 min of Anoxia and for a Moist Weight of Cerebral Tissue Equal to 100 g).

adequate provision of oxygen and nutrient substances; a basic exchange, i.e. the minimum exchange intensity needed for preservation of the biochemical superstructure of the neurons within the range of recoverability, when the oxygen intake and the intake of a nutrient substance are limited.

During the beginning stages of development, there is a decrease in the function exchange and in the exchange during complete rest for the animal, in comparison with what takes place in adult animals [2]. During development, the intensity of the exchange during complete rest for the animal in the central nervous system increases roughly twice (Fig. 3). The resistivity to anoxia, however, decreases during the same period by more than 12 times. Therefore, the intensity of the aerobic exchange during complete rest of the animal is not a determinant factor in the resistance of accelerations. During schemia, the single source of energy for the central nervous system is anaerobic glycolysis and the reserves of high-energy phosphate compounds. The intensity of the anaerobic glycolysis in immature nerve tissue is merely a fraction of the exchange intensity at a mature age (Fig. 3). Moreover, the anaerobic glycolysis has much more significance for the survival of immature nerve tissue than for a mature tissue. Its elimination (with the aid of monoiodoacetic acid) decreases the resistance of young individuals almost to the level of adult individuals, while this scarcely changes the resistance in adult animals (Fig. 4) [13]. /259

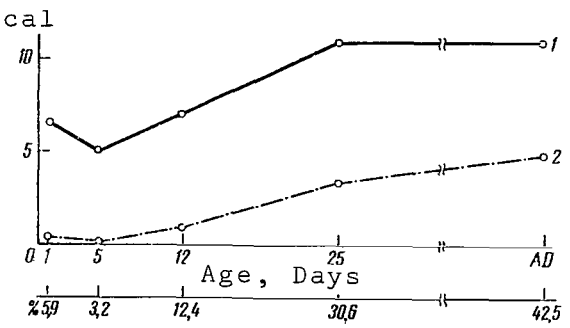

Fig. 4. Energy Exchange in the Brain, Calculated in Calories per minute of Anoxia, and for a Moist Weight of Cerebral Tissue equal to 100 g. (1) Aerobic Exchange in Vitro; (2) Anaerobic Exchange in Vivo. The Numbers Under Each Age are the Ratios Between the Aerobic and the Anaerobic Exchanges in Percentages (Aerobic Exchange = 100%.

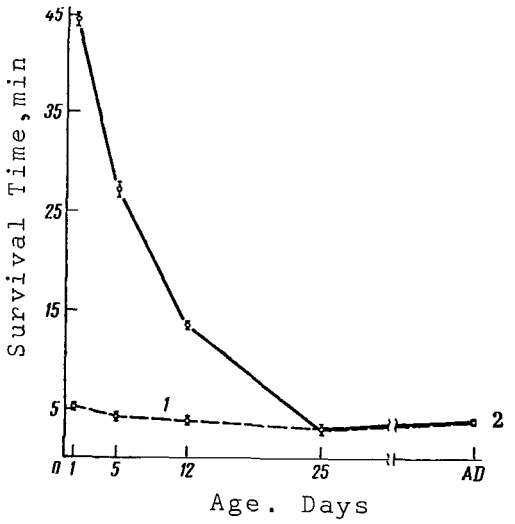

Fig. 5. Resistance to Stagnant Anoxis (Positive Acceleration) in Animals during the Administration of Monoiodoacetic Acid (1). (2) Control.

We should note that the accumulation of lactic acid as a product of anaerobic glycolysis occurs during ischemia in a manner which is parallel to the decrease in the carbohydrate content (Fig. 5). The balance of these substances is somewhat negative only for the newly-born animals. This indicates that immediately after birth there is an anaerobic type of exchange. This is also substantiated by the fact that administration of lactic acid increases the resistivity in the young individuals, and practically does not change it in the adults [3].

Therefore, the high resistance of the immature central nervous system to ischemia is caused by the following factors:

(1) Low intensity of the functional and basic exchanges.

(2) Low intensity of the basic anaerobic exchange.

(3) High capacity to use anaerobic glycolysis as a source of energy.

(4) The varying effect of catabolites of an anaerobic exchange on the exchange in the nerve tissue.

HISTOPATHOLOGICAL CHANGES IN THE CENTRAL NERVOUS SYSTEM CAUSED BY STAGNANT ANOXIA

The nature of the structural changes depends directly on the maturity of the nerve tissue. Vacuolization is a characteristic feature of ischemic changes at a young age [1]. During the maturation period for the higher divisions of the central nervous system, pyknosis of the ganglionic cells predominates. During a further development of the neurons, the pyknotic changes decrease, and vacuolization again predominates at a mature age.

In the immature tissue of newly-born animals, the vacuolization of the cells can be reduced to a certain degree. At a mature age, this leads to a decomposition of the nerve tissue. The pyknotic changes caused by ischemia in the young individuals are often reversible. The intensity of the ischemic structural changes and their prognosis must always be examined from the point of view of their development.

REMOTE AFTEREFFECTS OF STAGNANT ANOXIA OF THE CENTRAL NERVOUS SYSTEM

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Mammals can survive ischemia of the central nervous system if it lasts for a briefer time interval (recovery time) than a lethal effect (survival time). Younger individuals can endure ischemia of the central nervous system in relative and absolute relationships for a very long time, without any significant disorders. The older the animal, and the more differentiated its nerve tissue, the more serious and constant is the aftereffect for ischemia of the central

nervous system (Fig. 6) [4, 6, 9]. The aftereffect for prolonged ischemia in the newly-born can be recoverable to a greater degree than the aftereffect of a very brief ischemia for mature individuals. The relationship between the degree of the structural and functional adaptation is very complicated. A certain compensation of purely pathological changes in young individuals is accompanied by complete functional adaptation. The structural changes at the beginning of maturation of the higher parts of the central nervous system are rapidly and intensively compensated. However, they leave clearly pronounced and constant functional disorders in this case (Fig. 6) [1, 6].

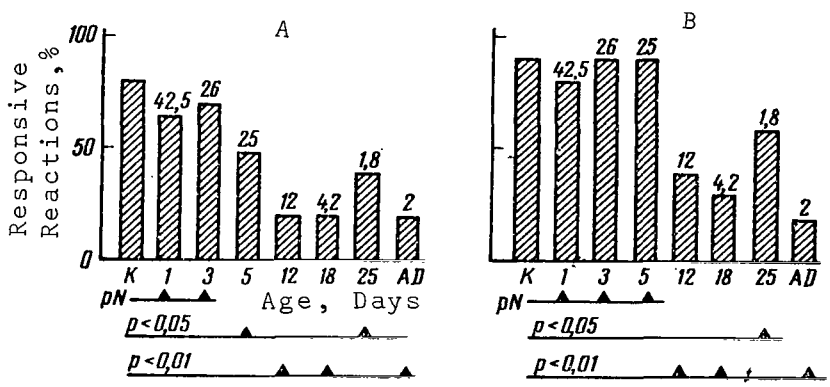

Fig. 6. Conditional Reflexes to Light (A) and their Extinction (B) in Rats which were Subjected to Stagnant Anoxia of the Brain during a Positive Radial Acceleration of 10 g (The Experiments were Conducted After 3 Months). The Numbers Over the Columns Indicate the Duration of the Ischemia of the Brain: K is the Control. Designations as in Figure 1.

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The rats were subjected to the effect of ischemia for 42 min, twice a day, at 6-hour intervals, beginning from the first day of of postpartum life. During the following days, the time for the effect was not made shorter, and this period was longer even on the second day than the survival time for the control animals.

The majority of the animals did not endure this effect on the sixth day, i.e. the duration of the ischemia exceeded that for the normal time of survival for the control animals of the same age by more than twice.

On the basis of these studies and our other studies [13], we can see that the adaptation of the exchange in the nerve tissue at the cellular level to repeated ischemia is possible during the period of early postpartum development (Fig. 7). Only the metabolic

adaptive processes can play a role in the development of ischemia, and they are probably linked with higher energy possibilities for anaerobic glycolysis in the young nerve tissue [4-6, 9, 12].

FACTORS WHICH AFFECT THE RESISTANCE OF THE CENTRAL NERVOUS SYSTEM TO STAGNANT ANOXIA

The resistance of the central nervous system to ischemia can be increased by decreasing the intensity of the exchange in the nerve tissue, and by the same requirements for oxygen supply and the nutrient substances and an increase in the inflow of nutrient substances to the nerve tissue before ischemia (It is possible that there are other substances with these biological effects).

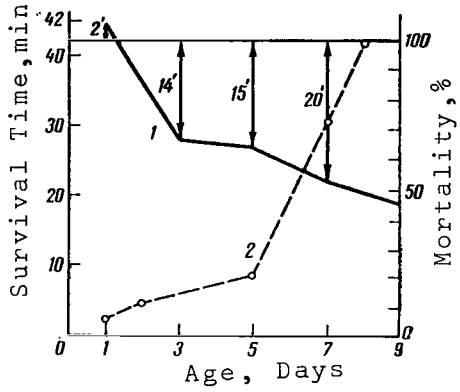

Fig. 7. Survival Time (1) and Mortality (2) for the Rats which were Subjected to Repeated Ischemia for 42 min from the First Day of Life.

The intensity of the exchange can be decreased, in particular, by hypothermia and pharmacological substances. During ischemia of the central nervous system, hypothermia and low temperature of the surrounding medium have a favorable effect throughout the entire ontogenesis. However, the relationship between the decrease in the body temperature and the increase in the resistivity is not absolutely linear [14].

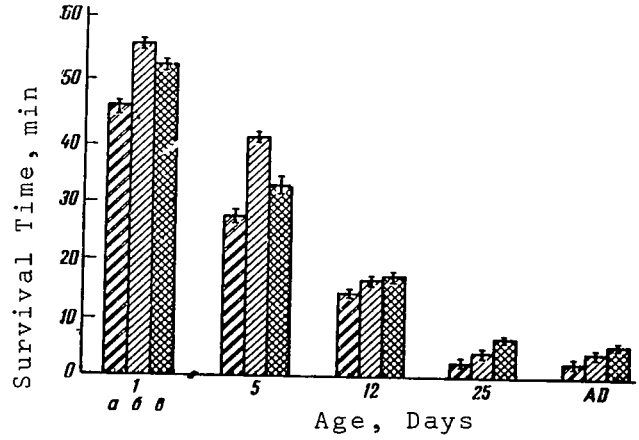

Fig. 8. The Effect of Chloropromazine and Pentobarbital on the Resistance of the Brain and Ischemia. (a) Control; (b) Chloropromazine (c) Pentobarbital /262

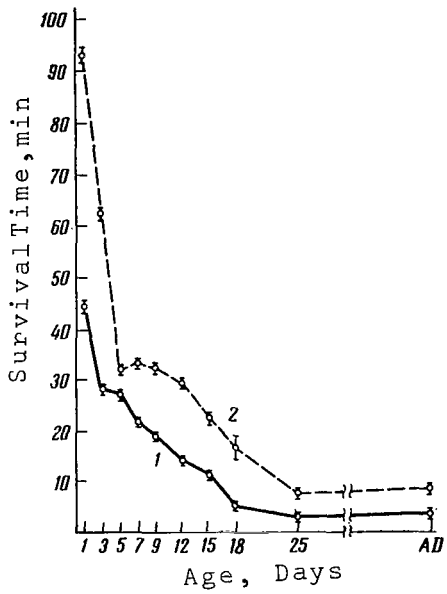

Fig. 9. Resistance to Stagnant Anoxia of the Brain during Negative Radial Acceleration (1) Positive Acceleration; (2) Negative Acceleration. Designations as in Figure 1.

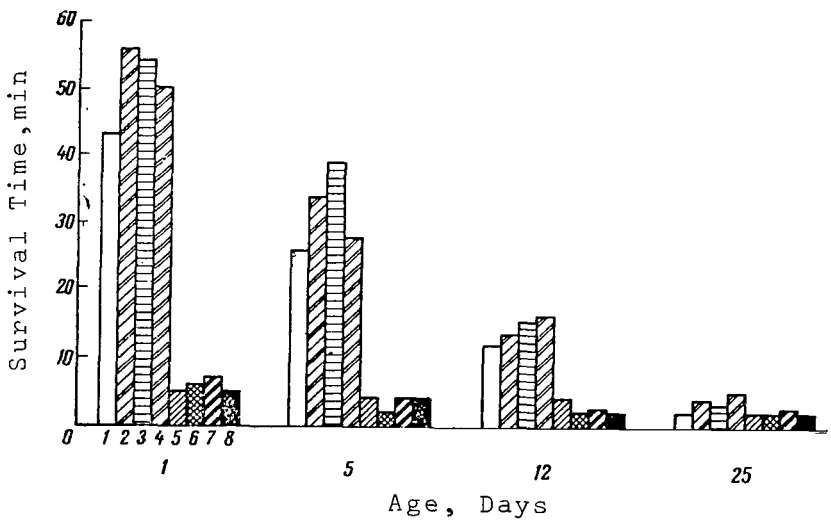

Fig. 10. The Effect of Suppressing Anaerobic Glycolysis on the Resistance to Ischemia (1) Control; (2) Hyperglycemia; (3) Chloropromazine; (4) Malonate (5) Monoiodoacetic Acid; (6) Hyperglycemia + Monoiodoacetic Acid; (7) Chloropromazine + Monoiodoacetic Acid; (8) Malonate + Monoiodoacetic Acid. /263

Chloropromazine and pentobarbital have a favorable effect on animals of all the age groups during ischemia. Chloropromazine has a greater effect on the immature tissues, and pentobarbital has a greater effect on the more differentiated tissues (Fig. 8) [11]. Their hypothermal effect is not a determinant, but a secondary factor.

Hyperglycemia (caused by administering glucose to the body of the parents) increases the resistivity to ischemia in all age groups. The greatest effect is observed in the youngest individuals [11]. The nerve tissue is more stable during negative acceleration than during positive (Fig. 9) [8].

The mechanism for the positive effect of various preparations and of hyperglycemia is indeed diversified, but it is certain that the anaerobic glycolysis plays an important part in it. The suppression of the anaerobic exchange (by means of monoiodoacetic acid) eliminates the favorable effect of these factors, in the youngest individuals in particular (Fig. 10) [12].

Having analyzed the reaction of the nerve tissue to stagnant anoxia, and prognosed and solved the problem of therapy for ischemia of the brain, it is always necessary to consider the degree of maturity for the development of the tissue in the central nervous system, as well as the type of disorder linked with the anoxia.

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X-RAY PHOTOGRAPHY OF THE HUMAN CHEST DURING ACCELERATIONS VARYING IN MAGNITUDE AND DIRECTION

K.I. Murakhovskiy

ABSTRACT: A description of the x-ray picture of the human chest is given on the basis of 36 experiments for the effect of transversely-directed accelerations with values from 2 to 12 g. The experiments were conducted in the direction of the summary vector for the acceleration, at angles of 65°, 80°, and 90° from the lengthwise axis of the subject's body.

On the x-ray photographs obtained, there is a decrease in the dimensions of the chest, a displacement of the diaphragm, characteristic changes in the transparency of the pulmonary areas, and complex dislocations of the heart and other organs of the mediastinum. A clear qualitative relationship is established between the above-mentioned changes and the magnitude and direction of the acting acceleration.

A rather limited number of studies have examined x-ray methods /264 for research under the conditions of prolonged acceleration, since their application involves a large number of methodological difficulties [10, 12-15, 19, 20].

The materials presented in this article show certain data on the qualitative and quantitative changes observed in x-ray photographs of the human chest during prolonged accelerations with values up to 12 g, acting in the direction "back-chest". The principal experiments were conducted for the direction of the summary vector of the acceleration at angles of 65° and 80° from the lengthwise axis of the subject's body. A few of the experiments were conducted with a strictly transverse (90°) direction of the summary vector of the acceleration. Thirty-six experiments were conducted in a centrifuge with a large radius, for an average rate of increase in the acceleration of 0.25 g/sec.

The x-ray photographs were made in the form of left lateral survey photographs of the chest during the phase of deep (and maintained) inspiration. We made two photographs in each experiment: the first was the background and the second was during the accelera- /265 tion, at the 15th second of "leveling".[1] In some cases, we made

[1]"Leveling: is what we call that period of the experiment during which a given value for the acceleration is preserved without changes.

control x-ray photographs during the period of the immediate after-effects (during the first to fourth minutes).

In the x-ray photographs obtained, we analyzed the degree of depression for the chest, the resting level for the diaphragm and the configuration of its cupulae, the area of the pulmonary field, the transparency of various regions of the pulmonary field and the pulmonary diagram, the position, shape, and contour of the cardiac shadow, the changes in the position of the organs in the mediastinum - the trachea, pulmonary vein, and aortic arch.

The measurements of the sagittal dimensions (distance in centimeters from the internal surface of the sternum to the anterior surface of the thoracic region of the spine) were conducted at three levels in the thoracic cavity: in the upper three, at the level D_3-D_4; in the middle three, at the level D_6-D_7; and in the lower three, at the level D_9-D_{10}. A decrease in this characteristic took place during an acceleration of 2 g (Fig. 1), and increased with an increase in the inertial forces. In each case, the greatest depression was observed at the D_3-D_4 level, which becomes understandable when we consider that the greatest mobility of the ribs is found in this lower region. Moreover, an increase in the depression of the chest at the D_9-D_{10} level occurred during an increase in the acceleration in relation to a greater gradient than at the other levels. In the experiments for the strictly transverse direction for the summary vector of the acceleration (angle of 90°), the depression of the chest and the rate of its increase, other conditions being equal, were greater than for angles of 65 and 80°. Thus, for example, for an acceleration of 6 g at an angle of 90°, the sagittal dimensions decreased in steps by 0.5-1.0; 1.5-2.0; 2.0-2.5 cm, while, for the same 6 g and an angle of 65 or 80°, it decreased by 0.0-0.5; 1.0-1.5; and 1.5-2.0 cm. For a value of the acceleration of 12 g, there was the same relationship: the depression of the chest in the experiments with the 90°-angle were equal to levels of 1.5-2.0; 3.0-3.5 and 4.0-4.5 cm, while, in the experiments with angles of 65 and 80°, it was 1.0-1.5; 2.0-2.5; and 3.5-4.0 cm, respectively. In relation to this, it would not be a great mistake to consider that the depression of the chest in the sagittal direction occurs in proportion to the magnitude of the inertial forces which act in a strictly perpendicular direction to the lengthwise axis of the subject's body. We can also agree with the idea that the cause of the

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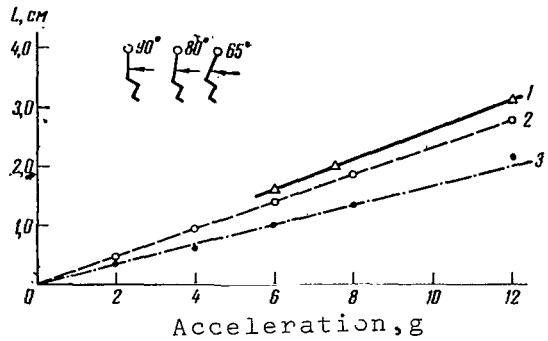

Fig. 1. Value for the Decrease in the Sagittal Dimensions (L) of the Chest during Accelerations of Varying Values. (1) Angle of 90°; (2) 80°; (3) 65°

deformation of the chest is the increase in the "weight" of all the anatomical elements in the walls of the chest as a result of the accelerations [1].

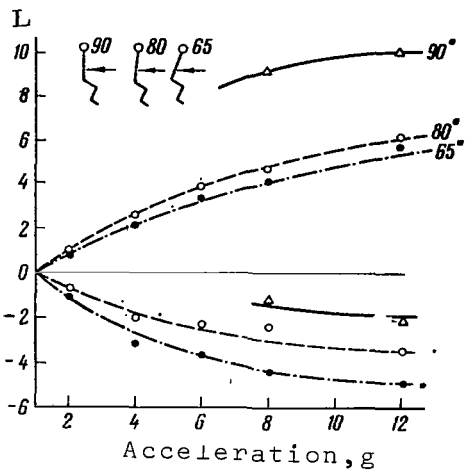

Fig. 2. Relationship Between the Resting Level of the Diaphragm and the Diaphragm and the Magnitude of the Acceleration for Various Angles of Inclination of the Trunk

The height of the diaphragm's resting level was the second parameter we studied; this characterized the change in the shape and volume of the thoracic cavity. We should note immediately that the changes in the left and right cupulae of the diaphragm, in all cases of the effect of the acceleration, had a principally identical character. The principal difference was noted only in the fact that the amplitude of the dislocations for the right cupula was always less than for the left. We can consider that the cause for this is the greater mobility of the left cupula of the diaphragm [4, 6, 9].

In all the experiments, we noted an increase in the resting level for the posterior region of the left cupula of the diaphragm, and an increase in the degree of its convexity, which could be caused by an increase in the intra-abdominal pressure as a result of the dislocation of the anterior abdominal wall. These phenomena increased progressively with an increase in the acceleration. In the cases when the values for the accelerations were identical, the greatest height for the resting level of the posterior region of the diaphragm and its greatest convexity were noted in the experiments with 90° angles.

The anterior region of the diaphragm took up a lower resting level in most cases, in comparison with the original, and was depressed. On individual x-ray photographs, the shape of the anterior region of the diaphragm seemed to repeat the contour of the nearby cardial shadow. With an increase in the acceleration, the downward movement of the anterior region increased. /267 The relationship between this phenomenon and the angle of the acting acceleration had a recoverable nature in comparison with the posterior region of the diaphragm. What we mean is that, all other conditions being equal, the anterior region of the diaphragm changed to a lesser value in the experiments with the 90° angles than in the experiments with angles of 65 and 80°. Moreover, it was noted that the relative movement of the anterior region of the diaphragm downward was usually less than the rise of the posterior region. The changes described

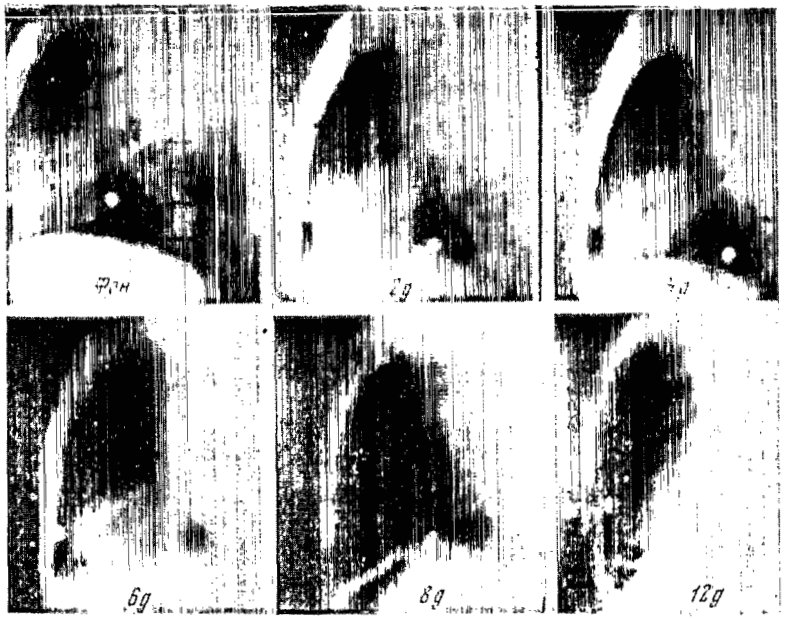

Fig. 3. X-ray Photographs of the Chest of Subject K during Accelerations of Varying values, Angle of 80°.

were caused by the dependence which is inherent, as is well known, in all elastomers (Fig. 2).

The evolution of the area of the pulmonary field was a demonstrative characteristic of the decrease in the volume of the chest, and thus in the volume of the lungs. Thus, in the experiments with the 65° angles, the area of the pulmonary field during accelerations of 2 g was 97% of the original; for 4 g, it was 97; for 6 g, it was 94; for 8 g, it was 93; for 12 g, it was 87%. In the experiments with the 80° angles, it was 95% for 2 g, 93 for 4 g, 93 for 6 g, 91 for 8 g, and 79% for 12 g. Finally, in the experiments with the 90° angles, it was about 90% for 6 g, 71 for 8 g, and 65% for 12 g.

It is well known that the effect of transversely-directed accelerations along the axis "back-chest" hinder mainly the inspirational movements of the coastal-muscular apparatus in the chest [2, 3]. The results of this study showed in this regard that the critical significance of the function of the principal components of the biomechanics of the act of respiration is found in the value of the inertial forces acting perpendicular to the lengthwise axis of the body. The inertial forces in this direction prevent the principal inspirational movements of the ribs in the sagittal plane, and lead to a sharp deformation and dislocation of the resting level for the diaphragm.

In all the cases for the effect of an acceleration, beginning with values of 2 g, there was a typical picture for the increase in the transparency of the anterior regions of the pulmonary field. This was particularly pronounced in the retrosternal region. In this case, there was also a decrease in the transparency of the posterior regions of the pulmonary field (Fig. 3).

The changes mentioned progressed significantly with an increase in the acceleration all the way to a notable clearing up of the pulmonary field and a complete disappearance of the pulmonary diagram in the anterior regions during accelerations on the order of 8-12 g, and an equally sharp increase in the transparency and an almost complete lack of differentiation for the elements in the pulmonary diagram in the posterobasal regions, beginning at values of 4-9 g.

The picture described characterizes primarily certain hemodynamic disorders in the lesser circulation, linked with the redistribution of the blood by the effect of transversely-directed accelerations [11, 15, 17]. Moreover, the studies in the literature indicate that the above-mentioned changes in the posterobasal regions of the pulmonary field do not eliminate the presence of tiny segments of an atelectatic drop in the pulmonary tissue in this region [8, 16, 18]. /268

Having evaluated the disorders in the shape of the chest (Fig. 4) and the characteristic changes in the hemodynamics of the lesser

circulation, we should now speak about the disadvantageous after-effects of these changes on the functional capacity of the respiration system. Unfortunately, the existence of only one lateral photograph makes it impossible for us to give a numerical evaluation of the decrease in the accumulation of air in the lungs. However, direct measurements of the characteristics for the external respiration, taken in our laboratory, gave rather reliable data regarding this relationship [1-3].

In order to calculate the effect of the acceleration on the shape, size, and position of the heart, we made a visual evaluation of the changes in the contour and density of the heart shadow, considered the changes in the distance from the base of the arch of the aorta to the apex of the heart (length of the heart), and measured the width of the retrosternal and retrocardial spaces. The cross-sectional dimensions of the heart shadow could not be obtained because of the projected superposition of its posterior contour on the shadow of the diaphragm during the moment of acceleration. In most of the experiments, there was a depression of the anterior contour in the heart shadow, and a progressive decrease in its density with an increase in the acceleration, which is an indirect sign of a decrease in the hyperemia of the cardiac cavities.

These symptoms were determined most clearly at accelerations with values on the order of 6-8 g. The degree of their intensity could not be determined in terms of their relationship to the direction of the total vector for the acceleration.

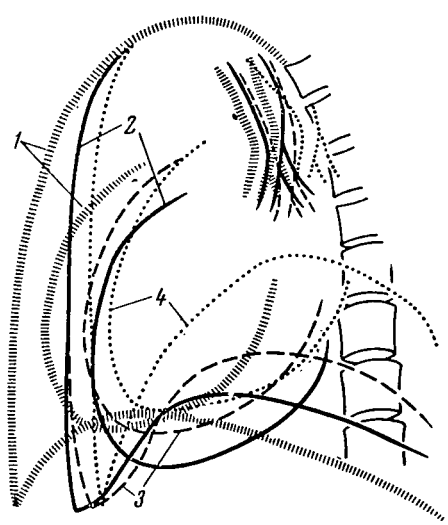

Fig. 4. Schematic Diagram of Changes in the Human Chest as Shown by X-rays During the Effect of an Acceleration of 12 g Along the "Back-Chest" Axis. (1) Background; (2) 65°; (3) 80°; (4) 90°

A comparison between the dimensions of the heart shadow during the moment of the effect and its dimensions on the background x-ray photographs (in the presence of only one characteristic - the length of the heart) did not show any significant changes.

In all the cases of acceleration, beginning with 2 g, there /269 were clear disorders in the topographic relationship between the heart and the surrounding organs in the thoracic cavity. Of primary importance was the tendency of the heart to move dorsally, as revealed by an increase in the retrosternal space and a decrease in the retrocardial space. With an increase in acceleration, the magnitude of these changes also increased. Thus, in the

experiments at 65° and 80° angles, the retrocardial space decreased with the background equal to 4.0-4.5 to 3.0-3.5 cm for 2 g; 1.5-2.0 cm for 4 g; 1.0-1.5 cm for 6 g; 0.5-1.0 cm for 8 g, and practically zero for 12 g. In the experiments at 90° angles, this decrease occurred at a more rapid rate. The increase in the width of the retrosternal space with the increase in the acceleration from 2 to 12 g was confined within the range of 1.0-1.5 cm, and the rate of increase for these changes was very small. The latter circumstance depended on the fact that the retrograde movement of the heart occurred somewhat synchronously with the movement of the anterior wall of the chest. However, there was no complete parallelism in these phenomena, since the heart, being a more mobile organ, somewhat anticipates in its movement the dislocation of the thoracic wall by inertial forces.

On most of the x-ray photographs, there was evidence of a movement of the apex of the heart downward from the original level, which increased with an increase in the acceleration. The heart followed the anterior region of the diaphragm and seemed to be imbedded in it. Correspondingly, in the experiments at angles of 65 and 80°, this phenomenon was more pronounced than in the experiments at 90° angles. It is necessary to mention here that on all the x-ray photographs made during the moment of the effect, there were signs of a movement of the vascular bundle, the trachea, and the radix pulmonis in the direction of the effect of the total vector of the inertial forces.

In measuring the angle of inclination of the anatomical axis of the heart to the horizontal plane of the body, we did not find any clear relationship. The numerical data obtained varied within rather wide ranges, and were not very reliable for such a small amount of material. We can speak only of a general tendency toward a decrease in this angle during the effect of the acceleration.

Taking all the above-mentioned data into account, we can assume that the cause for the appearance of retrosternal pains in some cases during such accelerations is not only the movement of the heart itself and the stress on the mediastinal ligaments [15], but also the over-extension of the parietal covering of the pericardium. The latter, on one hand, follows the downward movement of the anterior region of the diaphragm, to which it is firmly attached; on the other hand, it follows the movement of the heart in the dorsal direction. It is also certain that the changes described have a definite effect on the functional capacity of the cardiovascular system [2, 3, 5].

In all the cases of the control x-rays made during the period of the immediate aftereffects (1-4 min), we did not observe a complete recovery from the imposed changes. Therefore, it even seemed /270
that the purely mechanical character of the change occurring in the subject during the effect of transversely-directed inertial forces remains for some time after the termination of these forces.

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CERTAIN CHANGES IN THE LUNGS OF DOGS DURING THE EFFECT OF SINGLE AND REPEATED TRANSVERSE ACCELERATIONS

Yu.N. Korolev

ABSTRACT: The lungs of 20 male dogs, subjected to single (12 units for 1 min) and repeated (from 3 to 12 units for varying exposures) transverse accelerations in the "chest-back" direction were examined. The changes detected (hemorrhages, inflammatory processes, etc.) in both series of experiments have a uniform nature, and undergo reverse development with time.

The accelerations occurring as a result of acceleration can /271
cause various morpnological and functional disorders in the body [1, 3, 4]. It has been established that resistance to accelerations is linked to a great degree with the condition of the organs of respiration. For certain values and times of effect, accelerations can cause disorders in the lesser circulation and in the function of the external respiration, which then leads to the appearance of deoxygenation of the arterial blood and development of hypoxia in various organs [8]. Individual morphological data also show a number of changes in the vascular system of the lungs (hemorrhagic foci, edemata, thromboses [4, 9]).

The problem of the necessity for training an organism in a centrifuge in order to increase its resistance to accelerations is very important. With repeated accelerations, there was a favorable effect in some cases, while the authors have shown the development of a cumulative effect in others [2, 6, 7].

The purpose of this article is to study the effect of single and repeated accelerations on the lungs in animals, and, in particular, to determine the value of repeated training sessions.

We examined 28 male dogs after the effect of transverse accelerations in the "chest-back" direction. Six intact dogs served as controls.

In Series I of the experiments, the animals were subjected to a single effect of accelerations with a value of 12 units for one minute.

In Series II, the animals were subjected to the effect of repeated accelerations of increasing values, beginning with 3 units and ending with 12 units, for several days. The time for their

effect varied for each value of the stress.

We used the following examination methods in the study: hematoxylin-eosin, azure eosin-II, the methods of Mallory and Van Heison, the Tenser-Wong method, and the Schick reaction with sampling of the amylose saliva.

The disorders on the part of the vascular system were characteristic for both series of the experiments during the early periods (30 min, 1 hour). There was a sharp plethora of the dorsal regions in the lungs in the animals. There were often hemorrhages at the pleural surface in the preradical zone and on the dorsal side.

Microscopic examination at certain intervals in the dorsal regions of the lungs revealed an intense plethora of the blood vessels, particularly the capillaries and the venules, which was more pronounced in the animals subjected to the repeated effect of accelerations. In some vessels, the endothelium became swollen and thickened; in some places on the vascular wall, it became vacuolized and sometimes underwent desquamation. /272

The perivascular connective tissue appeared loosened and edematous. The interalveolar septa were thickened, obviously because of the swelling and the plethoric blood vessels. The lumina of certain alveoli, contained an edematous liquid and desquamous epithelial cells with occasional leucocytes.

In the general picture for the changes, the presence of hemorrhagic foci, which were often located beneath the pleura, was characteristic. Their dimensions reached 1.5-2 cm only in isolated cases, and the majority of the hemorrhages had small dimensions. The lumina of the alveoli, the alveolar paths, and sometimes the bronchioles accumulated the formed elements of the blood. In the hemorrhagic foci, the basal membrane of the endothelium in the capillaries was thickened and showed a pronounced Schick-positive stain, which obviously shows the increase in its penetrability. Obviously, the small hemorrhages usually occur also as the result of increased penetrability in the basal membrane. At the same time, vessels with mechanical injury to their walls were sometimes observed in the hemorrhagic foci. The elastic fibers at the site of the defect were thickened and twisted, and were intensely stained by orcein. These changes were characteristic for ruptures of the elastic fibers. There were usually no extravasates found in the ventral regions of the organ. Many of the empty inactive capillaries were without formed elements of the blood. Moreover, there was an expansion of the alveolar lumina, which is obviously a sign of an adaptative reaction.

In the lungs of the animals which were subjected to the repeated effect of accelerations, we observed (after the last rotation) both fresh hemorrhages and hemorrhagic foci with hemolytic erythrocytes, among which were found macrophages and segmental-nuclear

leucocytes. Similar "old" hemorrhages probably occur before the effect of the last acceleration.

The plethora of the lungs decreases within 24 hours. It is expressed in a non-uniform manner, and usually is preserved in certain segments of the dorsal regions and in the preradical zone of the lungs. Against the background of the vascular disorders, around this period (but mainly within 3 and 7 days) there develop inflammatory processes, whose degree varies at certain points in the pulmonary tissue. Within one day, the inflammation phenomena appear mainly in the form of a leucocytal reaction. The segmental-nuclear leucocytes infiltrate the tissue of the interalveolar septa and fill the lumina of the alveoli.

Around the 3-7th days, the inflammations acquire a more pronounced character, and take up a larger area in the pulmonary parenchyma. The exudate of similar focal pneumonias usually contains an /273
abundant quantity of neutrophilic leucocytes and macrophages (Fig. 1). The interalveolar septa are swollen, and the blood vessels are dilated. The lumina of the bronchi are filled with exudate. The mucous membrane is usually infiltrated with leucocytes, and desquamation of the epithelium is observed at separate points.

Moreover, in the lungs of the animals which were subjected to the repeated effect of accelerations during these periods, there are observed tiny foci with a fibroblastic phase of inflammation. The macrophages and the fibroblasts at these points are located in the interalveolar septa and the alveolar lumina.

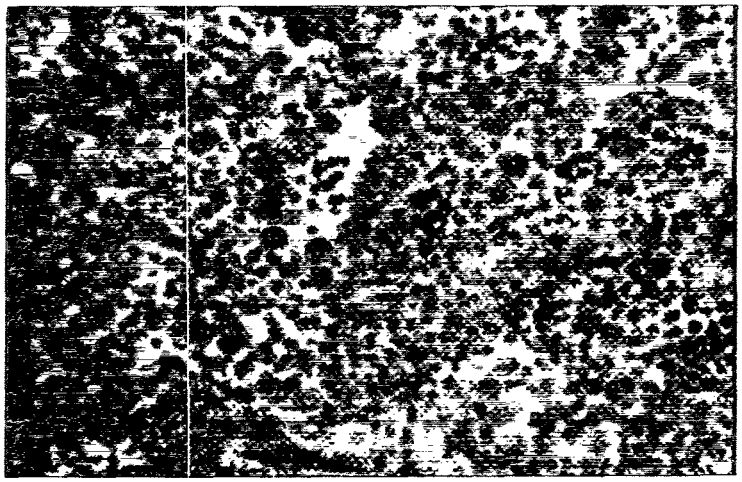

Fig. 1. Pulmonary Parenchyma Within 7 Days After a Single Effect of Accelerations. Pneumonia. Leukocytes in the Exudate (Principally Neutrophylia and Macrophages). Staining with Hematoxylin-Eosin, 300X.

During the following periods (15th-60th days), all changes undergo reverse development, and the histological structure of the lungs is recovered. At the same time, there are observed tiny foci of changed structure at separate points in the pulmonary parenchyma. Thus, the microscopic limited foci found in the growing connective tissue are beneath the pleura in most cases. At these points, the interalveolar septa, and sometimes the lumina of the alveoli, are filled with collagen fibers (Fig. 2). The elastic fibers are mostly found in the form of single fragments.

In comparing these series of experiments, we can note that the /274 foci of growth of the connective tissue are very often found in animals which had been subjected to the repeated action of accelerations. In this case, the productive phase of the inflammation is observed even in the immediate periods, which shows the possibility of a change in the lungs due to the effect of the first accelerations.

Fig. 2. Segment of a Lung with Expansion of the Collagen Fibers in the Interalveolar Septa, within 30 Days After a Single Effect of Acceleration. Staining by the Mallory Method. 300X.

The factual materials obtained show that single and repeated stresses in a certain regime can cause changes in the lungs, involving the vascular system and the parenchymatous structures. The observed changes are compensated by the organism, and undergo reverse development with time. The dynamics for the development of the disorders in these two series have definite differences in relation to the fact that repeated accelerations can cause definite changes in organ structure in both of them. However, these changes are of the same type.

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THE EFFECT OF TRANSVERSELY-DIRECTED ACCELERATIONS ON THE FUNCTION OF THE KIDNEY

P.V. Vasil'yev, V.F. Vasil'yeva, M.G. Zaks, Yu.V. Nadtochin, and M.M. Sokolova

ABSTRACT: In experiments on 7 dogs, with their ureters extended by the L.A. Orbeli method, the authors examined the effect of transversely-directed stresses with values of 5, 8, and 12 units on the function of the kidneys. It was established that, by the effect of these accelerations, there develops a slight osmotic diuresis, an increase in the excretion of sodium and potassium, and certain other divergences from the norm which have a brief duration. The possible mechanisms for the changes observed, among which the activation of the hypothalamic-hypophyseal system by the effect of the accelerations is of primary significance, are discussed in this article.

Despite the large number of studies examining the effect of accelerations on animals and man, there is still practically no information in the literature on the nature of the changes in the function of the kidneys under these conditions. Nevertheless, the practical problems concerning the preparation and safety of space flights urgently require a compreshensive examination of the effect of altered gravitation on the functional conditions of various organs and systems. /275

The principal problems in this study were the examination of the effect of accelerations with varying avlaues on the functional capacity of the kidneys and the analysis of certain mechanisms involved in the changes which occur.

METHODS

The studies were conducted on 7 dogs whose ureters were extended according to the L.A. Orbeli method. The glomerular filtration was determined by clearance of inulin or endogenic creatinine. The chemical analysis of the creatinine was made according to the method of Bonsnes and Toski [1], and the inulin was analyzed by the resorcin method [3]. The maximum capacity for the osmotic concentration of urine was examined after keeping the animals from water and food for 1 or two days; in order to evaluate the water-excretory function of the kidneys, we administered an amount of water equal to 5% of the body weight into the stomach. The osmolar concentration of the

urine was analyzed by the cryoscopic method with the aid of a semiconductorized thermistor [2]. The concentration of sodium and potassium was determined on a Zeiss flame photometer. The quantitative evaluation of the individual aspects of kidney function was conducted according to formulas which were based on the principal of clearance [4]. On the day of rotation in the centrifuge, the urine tests were also subjected to the regular clinical analysis. /276

Particular attention in this examination was given to a study of the osmoregulatory function of the kidney. A number of indicators are usually used for quantitative characterization of this function. It is well known that the osmotically concentrated urine is formed from primary urine which is isotonic with the plasma of the blood. The essence of this process is that salt-free water is reabsorbed from the tubular fluid, and the salts and other osmotically active substances are excreted with the urine. In order to determine the quantity of osmotically free, "pure" water which is reabsorbed in the osmotic concentration of the urine, we calculated the conditional volume of the liquid in which all the substances extracted by the kidney should be dissolved. This value is called the osmolar clearance (C_{osm}) and is determined by the formula $C_{osm} = (U_{osm}/P_{osm})V$, where U_{osm} and P_{osm} are the concentrations of osmotically active substances in the urine and the blood plasma, respectively, and V is the diuresis in ml/min. Obviously, the quantity of water which is reabsorbed in one minute for the osmotic concentration of the urine (T_{H_2O}) is equal to the difference between that volume of the liquid in which these substances should be excreted with the urine (if the iso-osmotic substances were left in the plasma) and the real volume of the excreted urine: $T_{H_2O} = C_{osm} - V$.

The transversely-directed accelerations were reproduced in a centrifuge with an arm radius of 4.2 m. During rotation, the dogs were kept on their backs; the direction of the accelerations was "chest-back". The values for the accelerations and the time for their effect were close to those which are often used for examinations on human subjects. The rate of increase for the accelerations and the deceleration was equal to 1 unit/sec. The rotation in the centrifuge was continued at 5 units for 3 minutes at "leveling", 8 units for 3 minutes, and 12 units for 1 minute.

RESULTS AND DISCUSSION

In the preliminary period, we examined the background characteristics of the renal function for 2 hours, after which we produced the rotation in the centrifuge.

Indirect Effect of the Acceleration. After the effect of accelerations with varying intensity (5, 8, and 12 units), we noted pronounced changes, of the same type but varying degrees, in the renal function.

For example, immediately after an acceleration of 12 units,

we observed a brief oliguria, after which the diuresis was intensified. Urination increased significantly in comparison with the original level (Fig. 1), which, however, was linked neither with the increase in the glomerular filtration nor with the increase in /277 the reabsorption of the osmotically free water (Fig. 2).

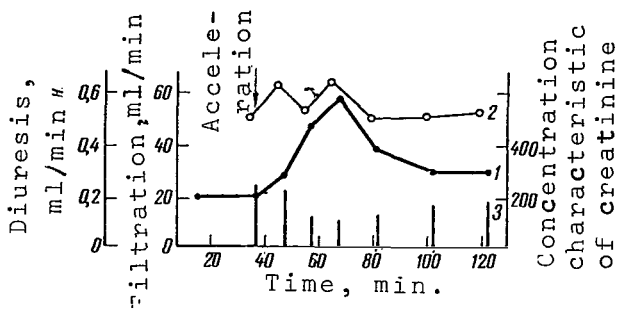

Fig. 1. Diuresis (1), Filtration (2), and the Concentration Characteristic of Creatinine (3) in Dogs during Accelerations of 12 units for 1 minute.

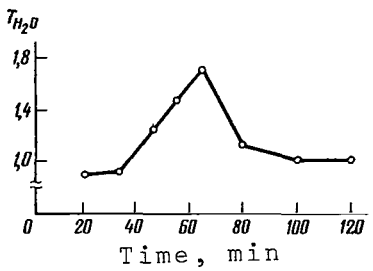

Fig. 2. Reabsorption of Osmotically Free Water During Acceleration.

An analysis of the data obtained shows that the increase in urination occurred according to a type of osmotic diuresis, and was caused by a decrease in the reabsorption of osmotically active substances (sodium and potassium salts, etc) and their excretion by the kidneys (Fig. 3,4,5). The increased diuresis coincided with an increase in the clearance of osmotically acitve substances and an intensification of the sodium and potassium excretion. For an analysis of the mechanism for the increase in urination, it is very essential that as the diuresis increases, so does the reabsorption from the tubular fluid of the osmotically free water (T_{H_2O}). These data indicate, in all probability, that the osmotic diuresis is developed against the background of a high level of secretion of the hormones of the posterior lobe of the pituitary, and that it is accompanied by an increase in the reabsorption of osmotically free water.

The essence of the intrarenal processes under the conditions of a developing osmotic diuresis can be found by comparing the change in the concentration characteristic of the creatinine ($\frac{U}{P}$cr) and the concentration characteristic of the osmotically active substances ($\frac{U}{P}$osm). These characteristics are the concentration

ratios between the substance in the urine being analyzed and its concentration in the blood plasma. According to the concentration /278 characteristic of the creatinine, we can determine by what factor the volume of the filtrate decreased in the process of uring formation. Since the glomerular filtration did not change, and the diuresis increased, the concentration characteristic of the creatinine decreased by the same factor as the diuresis increased. At maximum

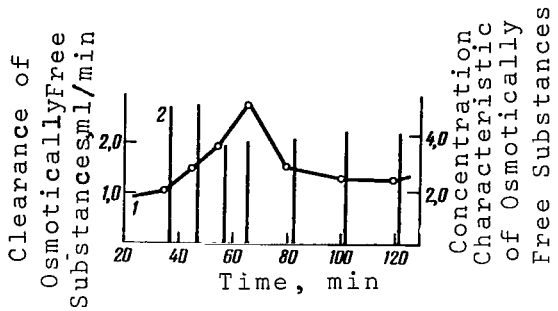

Fig. 3.

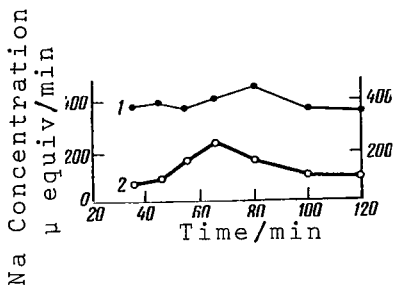

Fig. 4.

Fig. 3. Clearance of the Osmotically Free Substances (1) and the Concentration Characteristic of Osmotically Active Substances (2).

Fig. 4. Concentration of Sodium in the Urine (1), and Excretion of Sodium with the Urine (2).

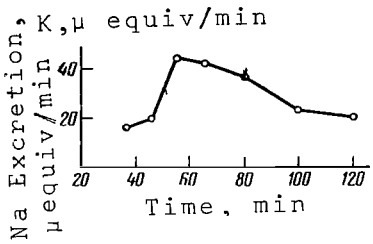

Fig. 5. Excretion of Potassium with the Urine.

diuresis, the concentration characteristic of the creatinine decreased from 230 to 113, while the urination increased from 0.28 to 0.58 ml/min. Very different ratios were characteristic for the $\frac{U}{P}$osm. At maximum diuresis, this characteristic decreased from 5.53 to 4.00. The relatively small decrease in $\frac{U}{P}$osm during the significant decrease in the $\frac{U}{P}$cr was linked with the fact that the diuresis was caused by a decrease in the reabsorption of the salts and the extraction of the water linked osmotically with them, while the reabsorption of the osmotically free water was maintained at a high level. Thus, all the data presented show that osmotic diuresis, and not water diuresis, is produced by the effect of the accelerations.

TABLE 1. KIDNEY FUNCTION IN DOGS DURING THE EFFECT OF ACCELERATIONS OF VARYING VALUES

Characteristics	Before Stress	After Stress of 5 units for 3 min	Before Stress	After Stress of 8 units for 3 min	Before Stress	After Stress of 12 units for 1 min
Diuresis, ml/min	0,06±0,01	0,1±0,02	0,11±0,01	0,14±0,01	0,15±0,04	0,26±0,05 $p<0,05$
Sodium Conc., µg-equiv/ml	178±59	185±47	133±11,18 $p<0,01$	215±23,2	146±35	197±25
Sodium Excretion, µg-equiv/ml	18,8±4,8	23,2±4,2	12,2±1,85 $p<0,01$	27,3±4,65	32,7±6,2 $p<0,01$	69,3±16,8
Potassium Conc., µg-equiv/ml	22,2±5,4 $p<0,05$	57±5,2	51±5,48 $p<0,05$	69±5,38	43±8,8 $p<0,01$	101±15
Potassium Excretion, µg-equiv/min	1,7±0,5 $p<0,02$	5,5±1,4	6,5±1,14 $p=0,02$	12,1±1,88	9,9±0,7 $p<0,001$	16,8±1,8
Conc. Characteristic of the Osmotically Active Substances	3,38±0,46	2,93±0,38	2,29±0,23 $p=0,001$	3,44±0,2	1,93±0,29	2,57±0,2
Clearance of the Osmotically Active Substances, ml/min	0,25±0,06	0,24±0,03	0,33±0,03	0,4±0,03	0,44±0,1	0,62±0,08
Reabsorption of the Osmotically Free Water, ml/min	0,19±0,05	0,18±0,01	0,2±0,015 $p=0,05$	0,28±0,021	0,14±0,02 $p<0,01$	0,28±0,04
Conc. Characteristic of Creatinine	499±20 $p<0,001$	296±41	194±14,9	211±13,9	113±27	127±17
Filtration, ml/min	27,6±3,0	25,9±1,7	24,4±0,76	26,5±0,87	29±1,5	30,2±1,3

NOTE: All the characteristics were calculated for one kidney. We considered the differences between the original characteristics and the effect of the accelerations to be reliable at $p \ll 0.05$.

Reaction to Accelerations of Various Values. The minimum changes in the renal function are observed after the effect of an acceleration of five units for 3 min (Table 1). Under these conditions, there is a brief increase in the excretion of potassium. With the effect of accelerations of 8 and 12 units, there is an increase in urination and excretion of potassium and sodium, and reabsorption of osmotically free water increases significantly. The diuretic reaction was even more pronounced after the effect of an acceleration of 12 units. /280

For all the animals, the renal function was completely normalized within an hour after the termination of rotation in a centrifuge.

The nature of the change in the value of the concentration characteristic of the osmotically active substances depended on the original diuresis. For the animals which were put on a dry diet before the experiment, and thus had a high level of osmotic concentration, the increase in the osmotic diuresis led to a decrease in the $\frac{U}{P}$osm. In those cases when the animals were given a normal ration and the concentration characteristic of the osmotically active substances had a small value, the $\frac{U}{P}$osm increased after the effect of the accelerations. This obviously is related to the difference in the effect of the antidiuretic hormone on the reabsorption of the osmotically free water and salts during uneven flow rate for the liquid by the nephron.

Study of the Water-Excretory Function of the Kidney. For the characteristic of the osmoregulatory function of the kidney, we conducted experiments with a water load. On the day when the animals underwent the accelerations in the centrifuge, obviously it was not expedient to conduct the test with the water load. The excretion of water could be limited because of the significant background activity of the antidiuretic hormone in the blood plasma Therefore, the water-excretory function of the kidney was examined the day before the acceleration and the day after the rotation in the centrifuge.

On the basis of the data obtained (which are given in Table 2), we can conclude that none of the imposed accelerations changed the capacity of the kidneys to excrete the water load; the renal function is not disturbed by the hypotonization of the urine, nor are the reabsorption of sodium and potassium from it, and other characteristics of the renal function.

Clinical Analysis of the Urine. During the period preceding the accelerations, there were no proteins in the urine. In the urine tests taken immediately after the rotation in the centrifuge, proteins were found in all the dogs. However, the amount of protwins (according to Roberts-Stol'nikov) did not exceed 0.13%. Within 2 hours, the proteins disappeared or were found only in traces (0.033%); on the following day, we could not find any proteins

in the urine. During a repeated acceleration, the proteins appeared again in the same quantities and just as briefly. In the urinary sediment, there were observed only single leucocytes, epithelial cells of the urinary tracts, and fresh non-lixiviated erythrocytes. The appearance of the erythrocytes, obviously, can be explained by mild mechanical injuries of the mucosa surrounding the openings of the explanted ureters. /281

TABLE 2. WATER-EXCRETORY FUNCTION OF THE KIDNEY IN DOGS DURING ACCELERATIONS OF VARIOUS VALUES

Characteristics	Norm	5 units	8 units	12 units
Percentage of Excretion of the Water Load in 60 min.	27.1±3,8	23,4±6,6 p>0,1	47,6±10,9 p>0,1	39,8±9,4 p>0,1
Na Conc. in the Urine at Height of Diuresis, μ-equiv/l	9,2±1,9	13,3±5,8 p>0,1	3,35±0,44 p>0,1	6,9±1,3 p>0,1
Minimum Value for the Conc. Characteristic of the Osmotically Active Substances, arbitrary units	0,26±0,02	0,31±0,05 p>0,1	0,17±0,02 p<0,02	0,21±0,02 p<0,1
Clearance of the Osmotically Free Water at the Height of Diuresis, ml/min	2,92±0,19	1,81±0,35 p>0,1	2,9±0,44 p>0,1	2,71±0,43 p>0,1

NOTE: All the characteristics were calculated for one kidney; *p* was calculated by its relationship to the norm.

CONCLUSION

Under the influence of accelerations at the values studied the changes in the renal function had a brief nature and were not found within several hours after the stresses. An analysis of the results obtained allows us to assume that the changes which occur (slight osmotic diuresis, increase in the excretion of sodium and potassium) are related not to mechanical or other indirect effects on the kidney, but to the neuro-hormonic effects, in particular to the activation of the hypothalamic-hypophyseal system. We have good reason to assume that the imposed accelerations are not related to any significant changes in the function of the kidneys.

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MORPHOLOGICAL CHANGES IN THE KIDNEYS OF DOGS AFFECTED BY SINGLE TRANSVERSE ACCELERATIONS

V.V. Korolev

ABSTRACT: With the aid of histological and histochemical methods, studies were conducted on the changes in the kidneys of male dogs, occurring as a result of the single effect of transverse accelerations with a value of 8 units for 3 min. The morphological changes found during the initial periods had the form of disorders in the intrarenal blood flow, the appearance of small hemorrhagic foci, and the development of hypoxia of the renal tissues. These disorders coincided with the appearance of dystrophic changes in the epithelial cells of the renal tubules. The dynamics of these morphological changes, as expressed in their reverse development during later periods after the experiment, show that these disorders have a recoverable nature.

The information available in the literature concerning the /282
effect of accelerations on the kidneys and the excretory system is, on the whole, very limited. Thus, Senelyar and other authors, studying the effect of accelerations with small values (2.5 units) and durations on the kidneys of dogs, noted principally vascular changes which consisted in a significant plethora of the glomeruli, an expansion of the peritubular capillaries, and a venous plethora (all the way to a rupture of the venular wall). The changes in the tubular cells results in a disappearance of the tufts and the appearance of granular cylinders in the lumina of the tubules. However, these changes were described for an experiment on only one animal.

In another article, Senelyar and Leb'yer described the changes in the kidneys of dogs which had been subjected to positive accelerations of 2.5 units lasting generally from 10 to 60 hours. In animals which were examined within 2 days after the experiment, they found significant capillary and venous hyperemia, interstitial hemorrhages, and disorders in the lower part of the nephron. In a dog which was examined three months after the experiment, they found interstitial and glomerular sclerosis and intense degenerative disorders in the tubules of the nephron. The authors considered that the total of the effects from the rotation in the centrifuge led to a progressive disorder in the neurovascular tonus,

and to a gradual condition of passive increased hyperemia, caused by sclerotic and degenerative changes in the tubules of the nephron. However, these data, also, were obtained for a small number of animals, and during the effect of accelerations which were small in value.

There are indications that accelerations cause changes in certain physiological and biochemical characteristics of the renal condition. Slonim showed that, in physically strong men subjected to "fatiguing" accelerations in the "chest-back" direction, there is an increase in the minute volume of the urine (from 0.7 to 1.95 ml/min) and the rate of glomerular filtration (from 85.4 to 157 ml/min). The rate of excretion of the creatinine increases simultaneously (from 0.57 to 1.34 mg/min), while its percentage in the blood increases. /283

The purpose of this study is to examine the morphological changes in the kidneys of dogs which were subjected to the single effect of accelerations.

The experiments were conducted on 14 dogs, for single accelerations of 8 units for 3 minutes in the "chest-back" direction. The animals were killed by ether within 1 hour, and 1, 3, 7, 15, 30, and 60 days after the experiment was conducted. The materials were fixed in a 10%-neutral formalin solution, Carnot fluid, and Zenker formol by the Maksimov method, and mounted in paraffin or celloidin. The sections, with a thickness of 5 μ, were stained with azure II-eosin, hematoxylin-eosin and by the Mallory method; we studied the histochemical reactions for ribonucleic acid according to Brash, for mucopolysaccharides (PAS-reaction), and for fat-sudan III. We also studied 4 control animals.

Intrarenal Blood Circulation. Within 1 hour after the effect of the accelerations, we observed macroscopically pronounced plethoras of both kidneys. A significant dilation of the capillaries in the Malpighian corpuscles, of the periglomerular and peritubular capillaries, the arterioles and the venules, and of the minute veins in the cortex and medulla of the kidneys, can be determined microscopically. The basal membranes of the glomerular capillaries have an intensive schick-positive reaction. The changes are particularly intense in the juxtamedullary zone of the kidney. In addition to hyperemia of the cortex and medulla, there are tiny hemorrhagic foci around the renal parenchyma, which are most frequently found in the region of the vascular poles of the glomeruli and between the tubules. In addition to these hemorrhages, there are signs of diapedesic bleeding in the cavity of the Shumlyanskiy capsule, which are shown by the fresh erythrocytes found in them as well as in the tubular lumen of the nephrons.

The nature of the hyperemia in the cortex and medulla of the kidneys after one day did not differbasically from that described above. We should note, however, that the hyperemia of the capillaries

in the vascular glomeruli of the kidneys was more intense around this time; they sometimes expanded aneurysmally, and their lumina were completely filled with formed elements of the blood. The most pronounced plethora was maintained in the capillaries of the glomeruli in the juxtamedullary zone, which probably is linked with the inclusion of the juxtamedullary collateral blood flow (Fig. 1).

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Fig. 1. Aneurysmal Expansion of the Capillary Lumen of the Vascular Glomerulus in the Juxtamedullary Zone of the Kidney, One Day After the Effect of Accelerations. Schick-Reaction. Enlargement:600 x.

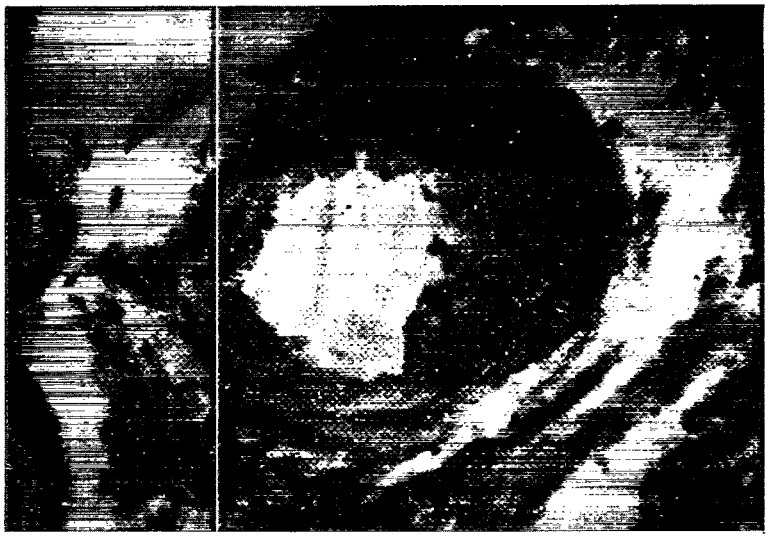

Fig. 2. Thickening and Loosening of the Subendothelial Layer of the Intima and Fatty Infiltration of the Tunica Media in the Vascular Wall of the Kidney, Three Days After Acceleration. Sudan III. Enlargement: 600 x.

By the third day, hemorrhages are no longer observed, and the /285 hyperemia of the cortex and medulla is insignificant. During this period, there are dystrophic changes in the walls of certain vessels in many cases: swelling and destruction of the endothelial cells, thickening and loosening of the subendothelial layer, and infiltration of the tunica media of the vessel with lipids (Fig. 2).

On the seventh day, there is still an insignificant expansion and plethora of the capillaries in the vascular glomeruli and in the peritubular capillaries. The dystrophic changes are also observed in the walls of the vessels, but they are more pronounced at the capillary level. These disorders lead to single cases of lipoid distrophy in the endothelium of the vascular glomeruli, mainly in the juxtamedullary nephrons.

During the following periods (on the 15th, 30th, and 60th days), the hyperemias of the vessels in the cortical and medullary substance of the kidneys are the same as in the control. The hemorrhages in the renal parenchyma cannot be found. There are remanent changes in the walls of the vessels: thickening of the basal membranes in the capillaries of individual glomeruli. There are areas of resorption at the sites of previous hemorrhages aroung the glomeruli and among the tubules of the nephrons.

Distrophic Changes in the Epithelium of the Tubules in the Nephrons. Within one hour after the experiment, there is observed an expansion of the lumen for the proximal regions of the nephrons, and detachment of the tufts at the apical surface of the cells. There are cells with pyknotic nuclei and basophilic cytoplasm in the walls of straight tubules, while there are forming cylinders in their lumina. In the expanded lumina of the distal tubules in the nephrons, there are fragments of disintegrating epitherlial cells and a basophilic homogeneous substance.

After one day, the dystrophic changes become more distinct in the distal regions of the nephrons and in the collecting tubules. In the distal regions, there is pyknosis of the nuclei, granular distrophy of the epithelial cells, as well as desquamation in the lumina of the tubules. The RNA content in the cells of the tubules is decreased. In the extended lumina of the collecting tubules, there are fresh erythrocytes and conglomerates consisting of the disintegrating cells in the vicinity of the nephrons found above (Fig. 3).

On the third day, the dystrophic changes in the cells of the distal tubules are preserved; they appear in the pyknosis of the nuclei in individual cells, in the vacuolization and desquamation of the epithelial cells in the lumina of the tubules, and in the expansion of the tubular lumina. In the epithelial cells of the direct tubules, we can observe vacuolization and lipoid infiltration of the cytoplasm.

Within 7 days, the epithelial cylinders and individual desquamous cells are still found in the lumina of the distal tubules. The epithelium of the direct tubules is vacuolized and contains fatty insertions.

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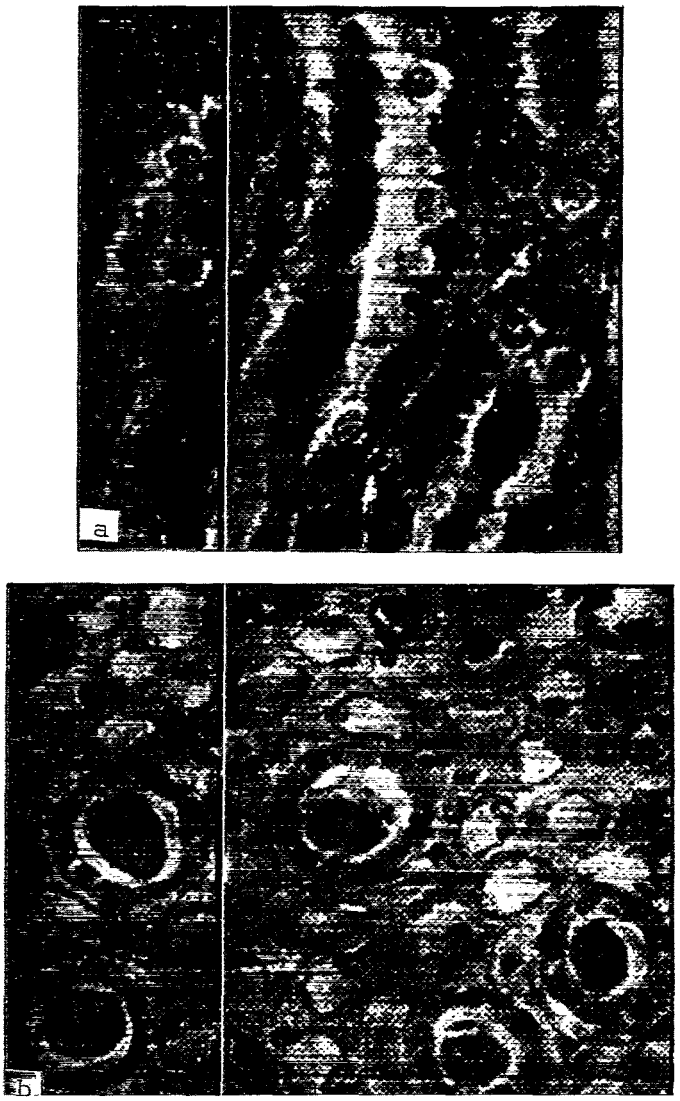

Fig. 3. Distrophic Changes in the Cells of Individual Nephrons (a) and Conglomerates of Desquamous Cells in the Lumina of the Collecting Tubules of the Medulla in the Kidney (b), One Day After the Effect of an Acceleration. Azure II-Eosin. Enlargement: 600 x.

During the following periods (on the 15th, 30th, and 60th days/287 following), the dystrophic changes in the epithelium of the tubules in the nephrons gradually decrease and disappear; only in the lumina of the distal tubules are there individual disintegrating cells with pyknic neclei.

CONCLUSION

The morphological disorders in the kidneys of the dogs are determined primarily by hemodynamic changes which occur as a result of the effect of accelerations. Actually, during the first hours and days after the experiment, there are changes in the vascular system: plethora of the glomerular capillaries (most often in the juxtamedullary zone), the veins and the venules, and also limited hemorrhages in the renal parenchyma. The penetrability of the wall in the glomerular capillaries is increased, as shown by the erythrocytes found in the lumina of the tubules in the nephrons. As a result of these vascular changes, there develps a conditon of hypoxia in the tissues, as well as a mechanical compression of the tubules in the nephron, with expanded vessels and eruption of blood. As a result of this, there are dystrophic changes in the epithelium of the tubules in the nephrons. The latter are expressed in the granular and lipoid dystrophy of the epithelial cells, a subsequent destruction of the individual cells, and their tearing away toward the lumina of the tubules. These changes appear after the first days and continue for a long period (up to 1-2 months). We should note that the greatest dystrophic changes appear in the cells of the distal tubules, which, according to a large amount of data in the literature, is the result of their high sensitivity to oxygen deficiency.

Therefore, the changes in the intrarenal blood circulation, and the dystrophic disorders in the epithelium of the tubules in the nephrons, appearing as a result of the effect of the accelerations, have a recoverable nature, since during the later periods there is a significant compensation of these morphological changes.

THE CONDITION OF THE LYMPH GLANDS IN ANIMALS DURING SINGLE AND REPEATED ACCELERATIONS

Yu. I. Afanas'yev and Yu. V. Mashkovtsev

ABSTRACT: An examination of the lymph nodes and spleen in dogs, after the effect of both single and repeated accelerations, showed that there are phase changes in lymphopoiesis in the lymph glands, in the activity of the reticular-endothelial system, and in the structural contracting apparatus of the spleen (which plays an important part in the deposition of blood in dogs). The degree of the changes in the lymph glands varies for both the animals in one series of the experiments and for the animals in different series.

In analyzing the changes in the lymph nodes and the spleen, special significance is given to the specifics of the functions of each of these organs in the dogs, as well as to the effect of various factors arising during accelerations (hypoxia, change in the neurohormone regulation, overexertion of the organs being studied by fluid deposition and redistribution of the blood).

The lymph glands have numerous functions (hemopoietic, protective, depository, etc.). They are very sensitive to every type of effect on the body, including accelerations. The available articles on the study of the lymphoid tissue during extreme stresses [1, 9], and on the relationship between the resistance to accelerations and the functional activity of the reticular-endothelial system [18, 19], confirm what we have said. /288

Considering the complexity of the structure and the functional features of the lymph nodes and spleen, we concentrated our attention on the study of the lymphoid follicles, the reticular endothelium of these organs, and the structural contracting apparatus of the spleen during accelerations.

METHOD

This study was conducted on dogs which were subjected to transverse (chest-back) accelerations varying in value and duration.

We established three series of experiments. In Series I, the acceleration had a value of 8 units for 3 minutes. In Series II,

the acceleration was 12 units for one minute. In Series III of the experiments, the animals were subjected to the effect of repeated accelerations of 3-12 units.

The experiments were conducted on 42 mongrel dogs. There were 14 dogs in each series. For control, we examined the organs of 4 intact dogs. The animals were killed by ether during various periods of the experiment - after 1 hour, and 1, 3, 7, 15, 30, and 60 days after the accelerations.

We cut out sections of the organ with a knife (across the spleen), using the ventral and dorsal ends of the spleen. These sections were fixed in Zenker formol and Carnot solution. The lymph nodes were taken from the left and right inguinal regions and fixed intact in the same solutions. The materials were mounted in paraffin. The sections were stained with azure II-eosin by the Unna-Pappenheim method and by the Mallory method for conjunctive tissue. We also tested the Thirman and Pearls reactions for iron. On the sections made perpendicular to the long axis of the lymph nodes, we measured the diameters of the reactive centers with the aid of an ocular micrometer. The area of the reactive center in the section was determined by the ellipse formula. We made a comparison between the average values for the area of the reactive centers for the experimental animals and for the control animals. We calculated the mitotic index in the reactive centers (the number of fissionable cells per 1000 cells in the reactive center). At the same time, we calculated the number of cells which underwent destructions. The latter were determined by the decrease in size, deformation, and compaction of the nuclei, and the change in their staining properties. For each animal, we examined at least 5000 cells in the reactive centers. /289

A series of experiments on 26 male rats, weighing 20-25 g, with accelerations of 36 units for 2 minutes, was conducted supplementarily. Three days, two days and 6 hours before killing 18 animals, we administered trypan blue intravenously (0.5%-solution per 0.5 ml). We examined the caudal para-aortal lymph nodes in the mesentery as well as the spleen. In 8 animals, we removed the mesenteric lymph nodes in order to examine them with an electron microscope. These animals were killed 6 hours and 1, 3, and 7 days after the experiment. Mice which were also treated with the same stains were examined on the third, seventh, and fifteenth days after the acceleration. For the control, we examined the organs of 6 mice.

The materials for electron microscopy were fixed according to Caulfield's method [10] and mounted in methacrylate. The sections were contrasted by Reynolds' method [16]. The photographs were made on a UEMV-100 electron microscope.

RESULTS

The spleen of the dog is among those organs whose predominant

functions involve the deposition of the blood [13]. In relation to this, the structural contracting apparatus is very strongly developed in the spleen of these animals, and the white pulp develops more weakly (in comparison with a spleen of metabolic type). Thus, the principal significance in the realization of the lymphopoietic function belongs to the lymph nodes. In turn, this function is not expressed uniformly in various groups of lymph nodes. It is most intense in the subcutaneous lymph nodes. In the mesenteric lymph nodes, the cortical substance (oymphoid follicles) is developed more weakly than the medullar substance, which can be explained by its high activity in carrying out phagocytic reactions and in depositing the lymph [4].

LYMPHOPOIESIS

The study of the lymphoid tissue in the inguinal lymph nodes of the control animals showed that the lymphopoietic processes occur primarily in the lymphoid follicles. The area of the reactive centers in the follicles varied from 0.021 to 0.038 mm^2 per section. The mitotic index in these animals was 16-23 (Figs. 1 and 2).

As we can see from the figures, there is a tendency for the mitotic activity in the animals of all the experimental series to decrease within one day after the acceleration. During later periods, there is a tendency for the mitotic activity to increase. The greatest increase in the number of mitoses in the reactive centers is noted on the fifteenth day after the experiment. In this case, there is an increase in the dimensions of the reactive centers because of an increase in the quantity of young elements in the lymphopoietic series. According to their type, the reactive centers can be determined as being the centers found at the active stage of lymphopoiesis (according to Maksimov and Blum). The tendency for

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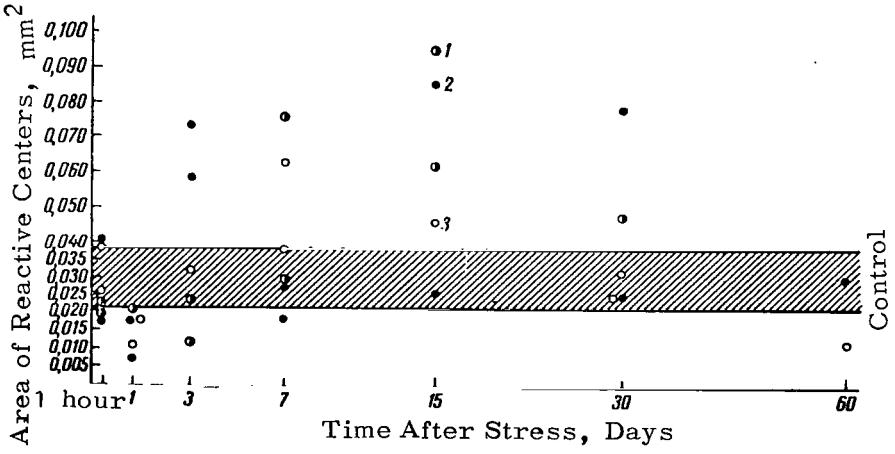

Fig. 1. Dimensions of the Reactive Centers of the Lymphoid Follicles in the Lymph Nodes After the Effect of Acceleration (1) Series I; (2) Series II; (3) Series III.

the mitotic activity to increase was most pronounced in dogs which underwent a single stress of 8 units for 3 minutes. On the 30-60th days after the accelerations, "resting" reactive centers are often found. The oscillations of the mitotic activity and of the areas of the reactive centers in the lymphoid follicles come close to the control level. /291

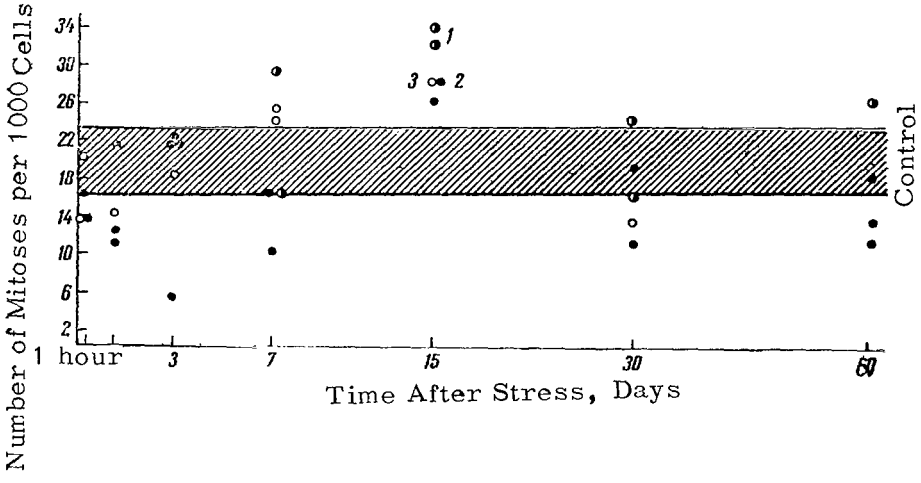

Fig. 2. Mitotic Activity in the Reactive Centers of the Lymphoid Follicles in the Lymph Nodes of Dogs After the Effect of Acceleration.

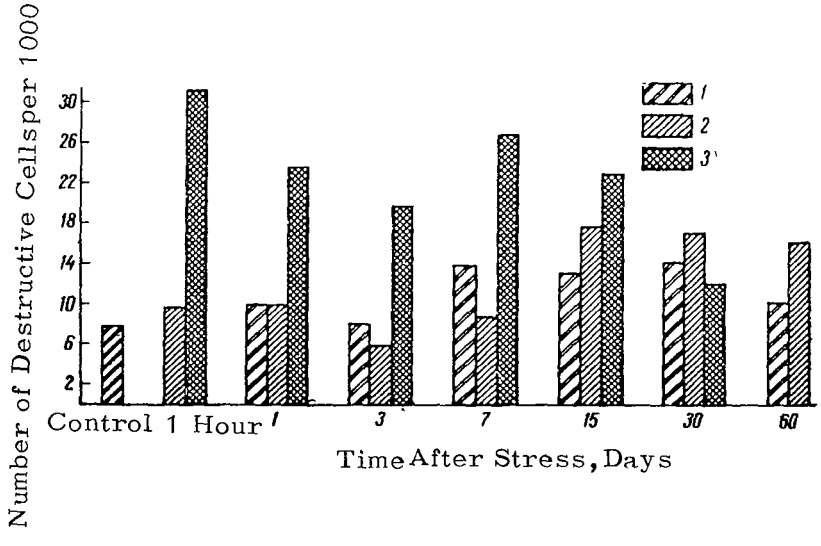

Fig. 3. Destruction of the Lymphoid Cells in the Lymph Nodes After the Effect of Acceleration. (1) Series I; (2) Series II; (3) Series III.

In addition to the mitotic activity in the nodes, we also examined the processes of cellular destruction (Fig. 3). For single accelerations, the quantity of destructive cells does not greatly exceed the control level. However, the study of the relationship between the processes of destruction and that of proliferation of the lymphoid elements shows a certain change in this relationship on the part of the two processes during the early periods after the experiments.

A sharp intensification of the destruction of the lymphoid elements is observed during repeated accelerations. The greatest quantity of cells with pyknotic nuclei was found within 30 minutes after the stresses (Fig. 4). Some such nuclei are encompassed by the macrophages of the follicles. An increase in the quantity of destructive cells was noted for 2 weeks after the stress. Around the thirtieth day after repeated acceleration, the processes of cellular destruction are almost the same as those for the control level.

The lymphoid follicles of the spleen, when affected by accelerations during Series I of the experiments, decrease in dimensions and are "liberated" from the small lymphocytes within 1 hour after /292
the beginning of the experiment. Then (up to 30 days after the acceleration) the follicles contain only a narrow border of small lymphocytes, and a large number of the follicles have large lymphocytes and lymphoblasts. Figures of mitoses in the lymphoblasts are

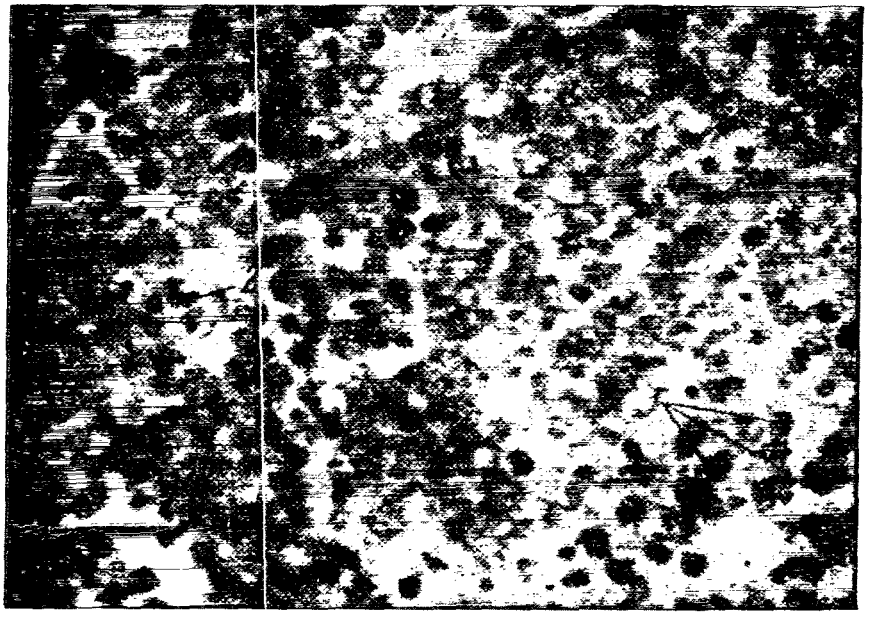

Fig. 4. Destruction of the Lymphocytes in the Lymphoid Follicles of the Inguinal Lymph Nodes by the Repeated Action of Extreme Stresses (1) Pyknotic Nuclei of Lymphocytes; (2) Macrophage with Fragments of Nuclei of the Lymphocytes in the Cytoplasm. Staining: Azure II-Eosin. 400X.

found very infrequently. At the end of the first month after the acceleration, "hyperchromic cells" intensively stained with azure-II are found in the lymphoid follicles of the animals in this series [1]. The cytoplasm of such cells contains a relatively small quantity of ribonucleic acid. The nuclei are lumpy, and similar to a dense accumulation of chromosomes. Obviously, such cells must be lymphoblasts in the stage of incomplete, abortive mitosis.

The white pulp of the spleen changed less regularly and gradually during Series II of the experiments. Within 1-3 days after the acceleration, the lymphoid follicles showed hyperplasia, and increased in volume. A large number of lymphocytes are also found in the red pulp, particularly along the trabeculae. Each trabecula seems to have a lymphoid vagina. The cytoplasm of many cells is highly basophilic, and contains a large quantity of RNA. Some cells in these lymphoid vaginae could undoubtedly be attributed to a plasmatic category. Within 30 days after the acceleration, certain lymphoid follicles are found to be free of small lymphocytes; in this case, almost the entire follicle consists of large lymphocytes and reticular cells. /293

In the case of repeated accelerations, the lymphoid follicles have clearly pronounced reactive centers whose width takes up half the diameter of the follicle within 1 hour after the termination of the last experiment. Large lymphoblasts (5-6 in one section

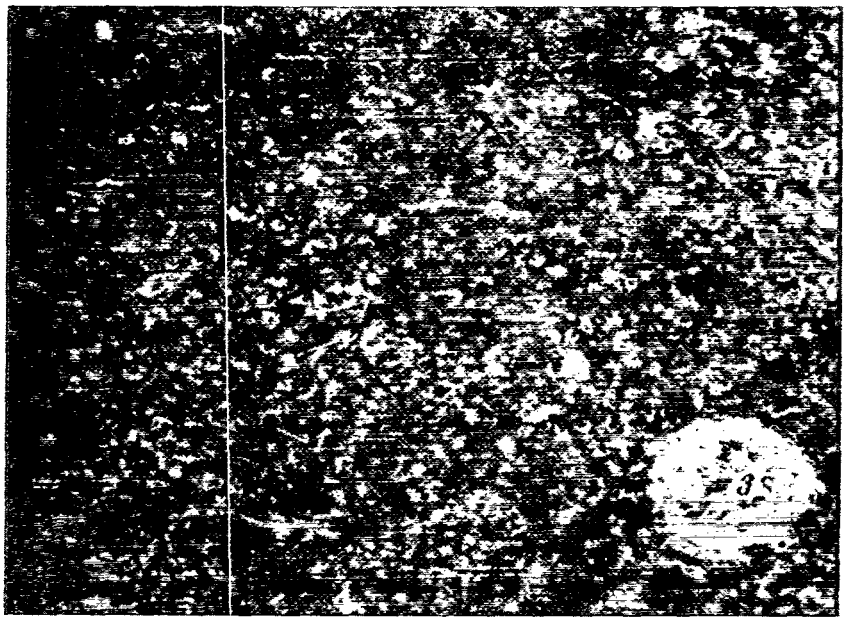

Fig. 5. Proliferation of Lymphocytes and Lymphoblasts in the Lymphoid Follicles of the Spleen in Response to the Repeated Action of Accelerations, 15 Days After Termination of the Experiments. (1) Mitotic Division of the Lymphocytes and Lymphoblasts; (2) Lymphoblasts; (3) Central Artery. Staining: Azure II-Eosin. 400X.

of a follicle) with an intensely pyroninophilic cytoplasm can be seen in the reactive centers. Moreover, in each reactive center there are 2-3 lymphoblasts or large lymphocytes, which are in a condition of mitotic division. The proliferative processes in the lymphoid follicles are intensified during the 15-30th days after the stress. The dimensions of the reactive centers in the follicles increase, and the number of lymphoblasts and dividing cells in them increases roughly 1.5 times, in comparison with the first hour after the termination of the last experiment (Fig. 5). There are fragments of degenerating lymphocytes among the dividing cells.

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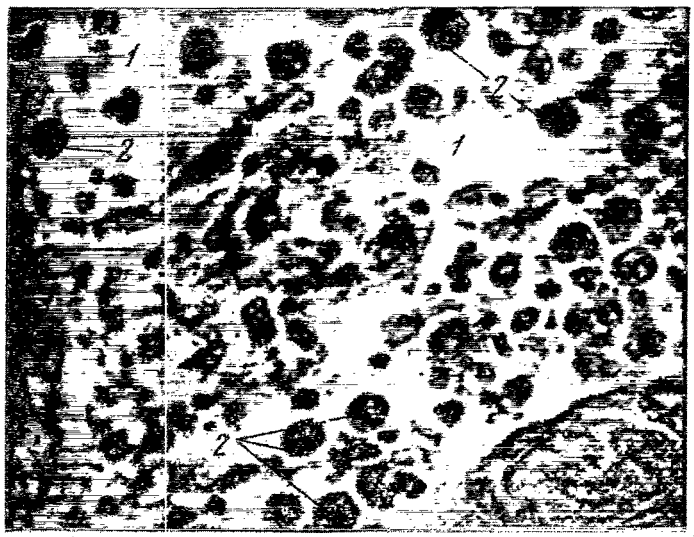

Fig. 6. Free Macrophages in the Sinuses of Inguinal Lymph Nodes Within One Hour After the Single Action of an Acceleration. (1) Intermediate Sinuses; (2) Free Macrophages with Phagocytic Fragments in the Blood Cells. Staining: Azure II-Eosin. 900X.

Within 2 months after the acceleration, the condition of the lymphoid follicles becomes the same as for the controls in all the series of experiments.

CONDITION OF THE RETICULOENDOTHELIUM

In the sinuses of the lymph nodes during the first periods after the acceleration, there is an increase in the number of free macrophages. In this case, we can trace the formation of the macrophages from the reticuloendothelial cells of the sinuses. The cells become rounded and their cytoplasm becomes hypertrophic. In the cytoplasm of single macrophages, we can see entrapped particles and sometimes even cells (erythrocytes and granular leukocytes) (Fig. 6).

During the first to third days after the acceleration, the

reaction to iron in the macrophages of the sinuses and the pulpy filaments gives a pale-blue homogeneous stain. This is more intense on the seventh day after the stress.

In the spleen of the animals in all the series of the experiments, even during the first day after the termination of the accelerations, there is an increase in the hemosiderin in the red pulp. The pigment is distributed both in the cytoplasm of the macrophages and between the cells (Fig. 7).

Later, after 15-30 days, the quantity of hematic pigment in the spleen decreases in all the series of experiments.

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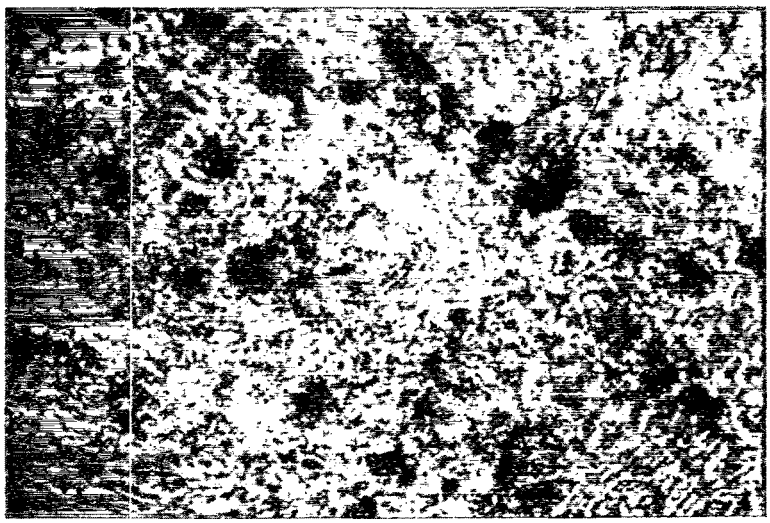

Fig. 7. Increased Quantity of Hemosiderin in the Macrophages of the Red Pulp with Repeated Action of Acceleration (30 minutes After the Termination of the Experiments). (1) Macrophages with Inclusions of Hemosiderin. Pearls Reaction. 400X.

A special examination of the absorptive power of the reticuloendothelium in mice which were subjected to accelerations of 35 units shows the activation of the processes of phagocytosis during the third to seventh days after the experiment. In the control animals, if the stain administered in vivo settles in the cytoplasm of the reticuloendothelial cells in the lymph nodes in the form of microgranules, within 3 days after the experiment, there are macrogranules and lumps of stain in these cells. A coarse granulation appears in the free macrophages. On the seventh day after acceleration, the processes of capture of trypan blue become even more intensified. In the cytoplasm of the macrophages, we noted the appearance of light vacuoles containing the stain. In certain cells, the stain fills up the entire cytoplasm, so that in this case it is

difficult to determine the nucleus (para-aortal nodes). Following this, the processes of the stain capture in the lymph nodes become the same as for the controls.

An electron-microscopic examination of the mesenteric lymph nodes in mice which were subjected to acceleration, but which did not receive stain, showed that the macrophages are in an active state 6 hours after the experiment: the quantity of micro-processes is increased, and there are many dense corpuscles surrounded by a single-edged membrane in the cytoplasm. These corpuscles have non- /296
uniform dimensions, and a matrix which differs in density. Their appearance is reminiscent of lysosomes [11]. At the surface of the processes, and in the depressions of the cell membrane, there are many micrograins with values of about 120 Å. Some particles of the same dimensions are seen in the cytoplasm of the macrophage fragments.

In the spleen of the control animals, no accumulations of the stain in the reticuloendothelium were observed. For the experimental animals, within 3 days after the acceleration, there were found only individual cells captured by the stain in the red pulp. After 7 days, the quantity of such cells increased. Following this, we continued to find macrophages with the stain in the spleen, although their number decreased.

STRUCTURAL CONTRACTING APPARATUS OF THE SPLEEN

During the microscopic examination of the spleen, the smooth-muscle cells of the capsule and the trabeculae were found to have undulant contractions in all three series of experiments. As a result, the trabeculae show expansion and stenosis. In addition to the contracted muscular cells, there are dystrophic changes in single smooth-muscle cells, particularly for the animals in Series II. Their cytoplasm becomes vacuolized and the nuclei are crumpled and tightened, with the vacuoles toward the periphery of the cell. These processes are most strongly pronounced after 3 days. For repeated accelerations, only single smooth-muscle cells undergo dystrophy, and most of the muscular cells are somewhat hypertrophic throughout the entire experiment. The hypertrophy of the smooth-muscle cells is also observed in the arteries. As a result of this, the trabecular and pulp arteries have a thickened muscular membrane and a twisted duct.

DISCUSSION

Single and repeated accelerations cause definite histostructural and functional changes in the lymphoid follicles, and activity of the reticuloendothelium in the lymphoid organs in the structural-contracting apparatus of the spleen in dogs. The changes detected are the result of a number of changes in the organism, occurring during the experiment. Some of these are hypoxia, a change in the neuroendocrine regulation, a redistribution of the formed elements in the blood during and after the effect of accelerations, etc.

The hypoxia during the accelerations, described by many researchers, can affect the condition of the lymphoid organs [3, 5, 8]. Thus, Meyer et al. [15], in their experiments on animals which underwent a decrease in the barometric pressure, drew the conclusion that the leucocytosis observed during the period immediately after the pressure drop was caused by a withdrawal of the blood from the deposit. The latter leukopenia is related to the functional depression of the bone marrow and the lymph nodes. /297

The phase changes we observed in the reactive centers of the lymphoid follicles during single and, in particular, repeated accelerations (decrease in the mitotic activity, intensification of lymphcytolysis), remind us of the condition of the lymphoid organs during stress reactions [17].

During a morphological examination of the adrenal glands in our dogs for Series I and II of the experiments, N. V. Militsina detected signs of a brief activation of the function of the cells in the nodular zone during the first hours after the acceleration. These changes were more expressed in the animals of Series I.

A. R. Kotovskaya et al.[1] observed an increase in the level of ketosteroids in the urine for the animals in Series III, during the first day after carrying out an entire complex of repeated accelerations.

An increase in the level of ketosteroids in the blood was also observed for the astronauts after their space flights [7].

As we know from the studies by Dougherty and others, the corticosteroids suppress mitosis of the lymphoid elements and accelerate their differentiating process; during the prolonged action of corticoids, there is karyorrhexis of mature lymphocytes [12].

A large number of researchers observed activation of the cells in the reticuloendothelial system during an increase in the blood level of the hormones in the adrenal cortex [20, 21]. Obviously, the same mechanism causes an increase in the absorptive power of the reticuloendothelium of the lymph glands in our experiments.

The intensification of the capture of hemosiderin by the Kupfer cells of the liver in the dogs of Series I and II, described by Ye. F. Kotovskiy, agrees with our data [6].

The change in the reticuloendothelium and the lymphoid follicles indicates, in our opinion, that the protective forces in the organism are mobilized during the effect of accelerations.

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[1] These data have not been published.

In the experiments we conducted, it was found that, for repeated and single accelerations, there is distrophy of single smooth-muscle cells in the structural contracting apparatus of the spleen. In addition to this, there is hypertrophy of the remaining muscular elements in the capsule, trabeculae, and vessels during repeated extreme stress.

Such a condition for the structural-contracting apparatus of the spleen can be explained, on one hand, by the contraction of the organ when the animals are kelled by ether and, on the other hand. by the extreme tension imposed on the spleen during acceleration. In our opinion, the latter circumstance can explain the dystrophic changes in the smooth-muscle cells.

The condition of the structural contracting apparatus is related to the function of the deposition of the blood and its liberation from the organ during the period when the organism requires an increase in the quantity of erythrocytes in the peripheral blood (for example, during a great amount of physical work, oxygen deficiency, etc.). Obviously, because of the hypertrophy of the smooth-muscle cells as a result of the repeated accelerations, the blood in the red pulp of the spleen empties out after the animals are killed, for almost all the periods of the experiment (except the first hour). At the same time, after single accelerations, there is plethora of the organ and a borderline state for the leucocytes, for the entire first week. Obviously, the latter is caused by the destruction of the endothelium in the vessels of the spleen [2]. /298

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PATHOMORPHOLOGICAL CHANGES DURING THE EFFECT OF RADIAL ACCELERATIONS IN THE "HEAD-FEET" DIRECTION

V.G. Petrukhin and S.S. Markaryan

ABSTRACT: Pathomorphological changes in the organs of dogs, occurring during rotation along the axis which passes through the pelvic area, at various angles of inclination for the trunk (0, 20, 70°), were examined. The results of the examinations showed that, for the effect of accelerations of 2.3 g and more at the level of the head, before the appearance of a "collapse" in the compensation of the cardiovascular activity, there are hemorrhages, edemata, and dystrophic processes in the cerebrum, myocardiu, lungs, and other organs.

At accelerations higher than 6 g, the animals sometimes die. The repeated effect of accelerations can cause dropsy, disintegration of the myelin fibers, and destruction of individual ganglionic cells in the cerebrum; in the heart, there are foci of micromyomalacia, and thromboses of the chambers in the right heart; in the lungs, there are foci of pneumosclerosis and emphysema; in the liver, there are signs of chronic stasis.

The effect of accelerations on an organism is of great interest /299 at this time, particularly in relation to problems of space exploration.

Despite the large number of physiological studies on the problem of tolerance to acceleration, the pathomorphological changes have not been discussed in great detail. The authors who have touched on these problems have often limited themselves to only macroscopic data [1, 2, 8, 10, 11, 13]. The histological changes in different organs have been discussed only in single works [3, 5, 6, 12, 14]. Nevertheless, a knowledge of the morphological data combined with the pathophysiological data could show the mechanism of the changes which occur in an organism during the effect of accelerations, which would be of great significance in working out rational methods for prophylaxis.

This examination was conducted on 22 experimental and 2 control mature dogs. The animals were put on a special rotating test-stand [7] and subjected to the effect of radial accelerations when the axis of the rotation passed through the pelvic area at angles of 0°,

20°, and 70°, from the axis of the trunk. In some experiments, the animals were subjected to a single acceleration; in other experiments, they experienced accelerations repeated twice, with intervals up to 30 min between rotations. Some dogs also took part in the experiments on the following days (up to 5 times). The magnitude of acceleration at the level of the head varied from 0.4 to 16.2 g. The duration of the effect varied from 1 to 20 min before the appearance of arrhythmia, extrasystole, or arrest of respiration - "collapse of compensation". Fourteen dogs died during the experiments, and the other 8 were killed during the periods after the accelerations - from 30 min to 12 days. Autopsies were made on all the animals. For the microscopic examination, we took fragments from the brain, lungs, heart, liver, kidneys, and adrenal glands. The sections were treated according to the methods which are generally used in histology.

For all the 12 animals which underwent the effect of a single acceleration, the morphological changes were roughly identical in nature, despite certain differences in the experimental conditions.

For the animals which died or were killed within 30 min after the experiment, there were small and large hemorrhages in the mucosa of the eyelids and in the anterior wall of the eyeball. The soft tissues of the head were plethoric and edematous. There were blood clots in the frontal sinuses, and less blood in the highmoritic sinuses. The sinuses of the dura mater were overfilled with blood. The pia mater was plethoric and edematous, while hemorrhages were /300
often found in the region of the hypophysis, optic chiasm, and occipital and parietal lobes. The medullary substance was plethoric and slightly edematous. The right auricle of the heart, the atrium cordis, and the ventricle were enlarged because of the accumulation of blood in them. The heart muscle was flaccid and anemic. The venae cavae were significantly thickened, and the pulmonary and hepatic veins were also enlarged in diamter. The other vessels did not change. At the dorsal surface of both lungs, often in the phrenic lobes and close to the radix, hemorrhages of various sizes were dispersed throughout. The liver was dense and extremely plethoric in section. The intestines, kidneys, spleen, and urogenital organs were usually hyperemic.

In dogs which were killed one day after the experiment, the appearances of plethora of the tissues were less pronounced.

A microscopic examination of the pia mater, revealed significant plethora, edema, and diapedistic hemorrhages. The veings of the medullary substance were expanded paralytically (particular in the white matter), and the capillaries were often clogged with lumped erythrocytes. Around most of the vessels, there was an edematous fluid, sometimes mixed with erythrocytes. The edema around the nerve fibers, microglia, and in particular the macroglia, was pronounced in all the regions of the brain. Certain ganglionic cells in the cerebellum, Ammon's horn, and cortex were more strongly

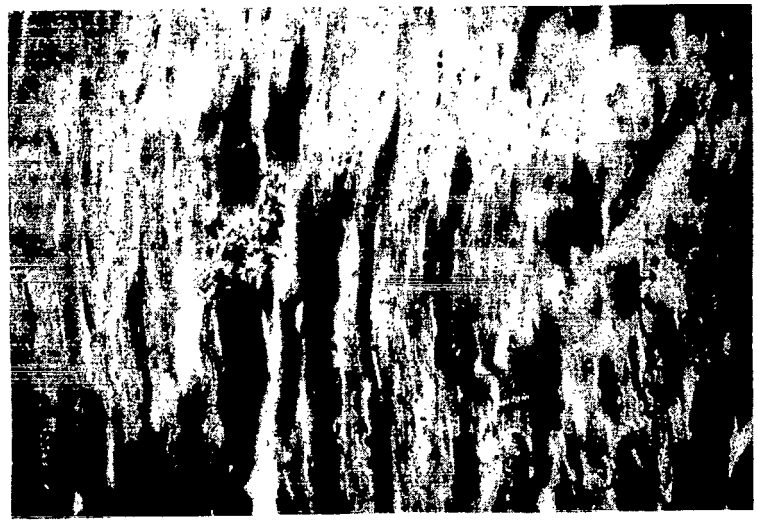

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Fig. 1. Eosinophilia and Swelling of the Muscle Fibers in the Myocardium of a Dog Following the Effect of Accelerations of 2.4 g for 17 min, with an Angle of Inclination of 90°, One Day After the Experiment.

Fig. 2. Lamination of the Elastic Fibers in the Arteries of the Lung, and Wide-Open Arteriovenous Anastomosis in a Dog, for the Effect of Accelerations of 14.5 g, with an Angle of Inclination of 20°. The Dog Died during the Sixth Minute of the Experiment.

stained with eosin and thionine, and the Nissl bodies were clumped. Other cells were enlarged and light, and their protoplasm contained vacuoles, while each nucleus had two nucleoles. For the animals which were killed one day after the experiment, in addition to what we have described, there were signs of resuscitation in the micrologia, reminiscent of the picture of a neuronophage, around certain injured cells of the cortex.

The arteries of the myocardium were often spasmatic, and their tunic adventitia and surrounding connective tissue had their fibers separated by an edematous fluid which contained an admixture of erythrocytes in places. The lumina of the capillaries often contained only single erythrocytes. Certain muscle fibers were swollen, lost their streakiness, were stained eosinophilically, and underwent fuchsinophilic dystrophy (according to Selye), and the quantity of ethmoid fibers in them decreased. Throughout the entire myocardium, the percentage of glycogen clumps decreased to a great degree. For the animals which were killed one day after the experiment, the changes in the myocardium were the same as those described above, but the edema in the intermediate tissue and the swelling of the muscle fibers were more pronounced (Fig. 1); the glycogen content in the myocardium was almost completely recovered. In three dogs, there was necrosis of some of the muscle fibers beneath the epicardium of the left ventricle.

In the regions around the radices of the lungs, foci of emphysema alternated with atelectases. Some arteries were spasmatic, and others were distended with blood. All the veins were expanded paralytically and surrounded by a border of edemata. The arteriovenous anastomoses were wide open (Fig. 2). The capillaries of the septa were clogged with erythrocytes. We often found hemorrhagic areas. In the lumina of certain bronchi, there was mucus or a small /302
quantity of an edematous solution. The latter was also found in the lumina of certain alveoli (Fig. 3). In the peripheral regions of the lungs, emphysema, with small segments of atelactases, predominated. Alveoli which were filled with an edematous fluid and erythrocytes were found more often. The animals which were killed one day after the accelerations showed increased hemorrhaging and edema. There were single leukocytes in the edematous fluid, while there were cells of desquamated epithelium in the alveoli.

In the liver, the veings of the peripheral regions were distended by blood, and certain arteries were spasmatic. The connective tissue layers surrounding the triad were edematous, and erythrocytes were often found in the edematous fluid. The intrastructural capillaries were distended with blood, and the central veins had a normal appearance. In the protoplasm of the hepatic cells in the central regions of the lobules, there were small basophilic granules or vacuoles. In the animals which were killed 30 minutes after the experiment, the vacuolic dystrophy of the heptic cells was more strongly pronounced. There was an iron-containing pigment in the Kupfer cells. In those cases when the dogs were killed after one

day, there were small droplets of fat in the protoplasm of the hepatic cells, against a background of pronounced vacuolar dystrophy. /303 The protoplasm of the bile ducts also underwent liphoid infiltration.

Plethora was noticed in the kidneys of the animals which died or were killed 30 min after the experiment. In those which were killed after one day, the epithelium of the distal regions in the twisted tubules underwent granular and vacuolar dystrophy.

In the spleens of animals which died, there was a plethora of the pulp and a decrease in the amount of lymphoid elements in the follicles. In those which were killed, there was hyperplasia in the reticuloendothelial cells and an accumulation of hemosiderin in the reticular cells of the pulp in the follicles, after one hour.

The percentage of lipoids in the protoplasm of the cells of the cortex in the adrenal glands for the animals which died or were killed after 30 min was roughly the same as for the control animals; in those which were killed one day after the experiment, there were almost no lipoids.

Two dogs underwent accelerations which were repeated twice, at intervals of 25 and 30 min. Both dogs died during the experiment. In contrast to the animals which died during the experiment involving single accelerations, the lateral ventricles of the brain were distended with fluid. Moreover, there were pronounced hemorrhages

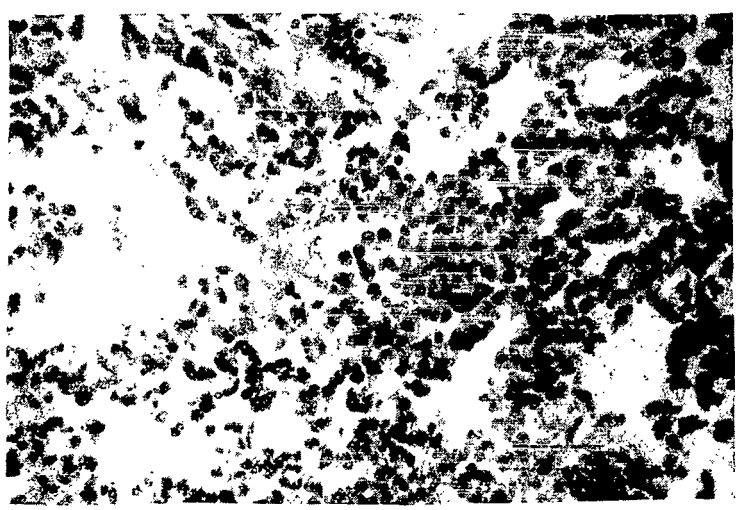

Fig. 3. Lung of a Dog Showing the Effect of Accelerations of 9.5 g, with the Angle of Inclination of 75°. The Dog Died during the Seventh Minute of the Experiment. The Capillaries of the Septa are Clogged with Erythrocytes, and there is Blood or an Edematous Liquid in the Lumina of the Alveoli.

beneath the pia mater, and, in one dog there was even a subdural hemorrhage in the anterior and posterior cranial fossae. During the microscopic examinations, the appearances of a disorder in the blood circulation were much more pronounced in these dogs; hemorrahges and edemata were also found more often and in large numbers. In the sarcoplasm of the muscle fibers in the heart, there were small droplets of fat. In the liver, the vacuolar dystrophy was more pronounced and there were signs of a beginning lipoid dystrophy.

Eight dogs underwent repeated accelerations up to 5 times. These accelerations differed in value, duration, and angle of inclination of the trunk to the axis of the rotation. The intervals between the tests were one to three days. Considering that the repeated effects, as a rule, were terminated when there were signs of a disorder in the cardiac activity according to the electrocardiograms (the "collapse of compensation"), we can conclude that most dogs tolerate greater stresses during the first effect than during subsequent experiments.

The pathomorphological changes in the organs of this group of animals were varied, and they depended mainly on the time from the moment of the last acceleration until death.

In those cases when the animals died during the experiment, the macroscopic picture for the changes corresponded to those found in the preceding group of animals. If the dogs did not die during the experiment, but were killed, the appearances of venous stasis disappeared around the third day, and the organs took on their regular appearance. Against this background in the lungs, pia mater, mucosae of the eyes, and frontal sinuses, we could easily find residual phenomena after previous hemorrhages (yellowish in color). Miliary dense fragments were scattered over the surface of /304
the pleura. The liver sections in certain animals had the appearance of nutmeg. In 3 dogs, there was a thickening of the walls in both ventricles of the heart. Moreover, all the dogs in this group showed a significant expansion of the ventricles in the brain, all the way to formation of dropsy (in 2 animals), thromboses of the right atrium (in 2 dogs), and scattered foci of pneumonia.

The microscopic picture for the dogs which died during the experiments was the same as for the preceding group of animals. In addition to this, in all the animals of this group (whether they died during the experiment or were killed), there were other changes, related to the remote afteraffects for the accelerations which they had endured previously: in the cerebrum, heart, lungs, liver, kidneys, and spleen.

In the pia mater, in the region around the basis of the cerebrum, there were focal accumulations of young connective cells. These cells sometimes contained hemosiderin grains in the protoplasm. In the cortex, Amman's horn, subcortical nodes, and cerebellum of the animals which were killed one to three days after the

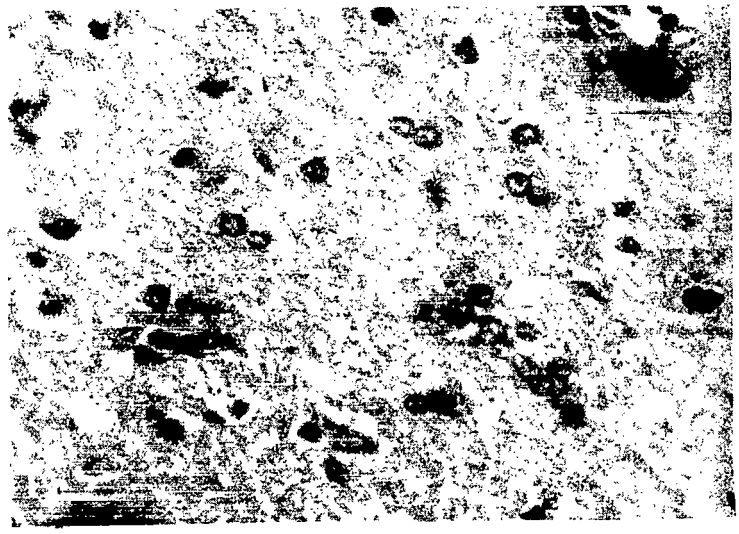

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Fig. 4. Cerebral Cortex of a Dog After Acceleration Repeated Three Times: on the First Day, 4.6 g for 20 min, with an Angle of Inclination of 75°; On the Fifth Day, 4.5 g for 5 min; on the Seventh Day, 3.6g. The Dog Died in the Seventh Minute of the Last Experiment.

Fig. 5. Organized and Rechanneled Thrombus of the Lung in a Dog After the Effect of Accelerations: First Day, 3.2 g for 20 min, with an Angle of Inclination of 75°; Third Day, 2.4 g for 18 min; Fourth Day, Increasing from 1.8 to 8.5 g for 8 min. Killed After 12 Days.

last experiment, certain ganglionic cells were wrinkled, with a protoplasm which was thickly stained with eosin or thionine, while other cells were swollen, with a poorly-visible Nissl substance and vacuoles in the protoplasm. Some of the cells were transformed into shadows; around them, we could see an accumulation of microglial elements (Fig. 4) which penetrated into the protoplasm at intervals (appearances of neuronophagia). In the animals which were killed after 7-12 days, the processes of wrinkling and neuronophagia predominated in the ganglionic cells.

Beneath the endocardium of the papillary muscles, in the right and left ventricles of the hearts of three dogs, there were foci of necrosis of the muscle fibers (varying in size and often laminated). Sometimes there was a scattering of subsequent leukonad histiocytic reactions. In the veins of the epicardium, there were often found fresh and organized thrombi. In all the dogs which were killed one day or more after the accelerations, the glycogen content was close to the norm.

In the lungs of all the dogs for this group, there was emphysema, including scattered tiny, and sometimes even large, foci of poorly-aerated tissue. The lumina of the alveoli in such segments were rimose, and the septi were thickened because of dispersion in them of argyrophil fibers and new connective cells which sometimes contained hemosid rin and dust-like particles in the protoplasm. The bronchi, as a rule, were spared, and their walls were thickened and infiltrated with lymphoid cells and histiocytes, in places with an admixture of leukocytes. An overgrowth of small bronchi and alveoli could be seen only infrequently. In individual veins, we found both fresh and organized and rechanneled thrombi (Fig. 5). Moreover, in 3 dogs, there were found foci of catarrhal-purulent pneumonia.

In all the animals, we cou d see expansion of the capillaries in the central regions of the lobules of the liver, while there were signs of liphoid dystrophy in the hepatic cells. Some dogs showed thrombosis of the veins in the liver.

The changes in the spleen led to a decrease in the magnitude of /306
the follicles and an accumulation of hemosiderin in the reticular cells of the pulp.

A decrease in the amount of lipoids in the protoplasm of the cells of the cortex in the adrenal glands was observed in animals which were killed before 3 days after the last effect. Around the 7-12th days, the percentage of lipoids in the adrenal glands had recovered.

In the kidneys of all the animals which died or were killed later than a week after the first effect, there was an increase in the number of cells (lymphoid and endothelial) around the conducting arteries. The glomeruli which were supplied by such arteries were

partly wrinkled. In the cortex we found lymphoid-cell infiltrates with an admixture of histiocytes.

Thus, the results of the pathomorphological examinations show that radial accelerations at values higher than 2.4 g, acting at the level of the head for 20 min, cause significant pathomorphological changes in the organism of the dogs, while at values greater than 6 g, the animals may die during the experiment.

Although each animal had a different tolerance to accelerations, the difference in tolerance for one dog in comparison with another nevertheless did not exceed 1-1.5 g. The dogs' tolerance to accelerations depends on the magnitude and duration of the latter and the angle of inclination of the trunk to the axis of rotation. The animals endure the accelerations much better when the angle of inclination of the trunk to the axis of rotation is 20° than when it is 90°. The difference in the magnitude of the acceleration in this case is roughly equal to 2.5-3 g.

Despite the varying conditions of the experiments, the pathomorphological picture for the changes in the organs was identical. In all the animals which died during the experiment, the disorder in the blood circulation was of primary importance during the autopsy: the stasis of the blood in the cavities of the right heart, in the vena cava, the liver, and the regions around the radices of the lungs; hemorrhages beneath the pia mater, frontal and highmoritic sinuses, in the retina of the eye and in the lungs.

In addition to the hemorrhages which can be seen by the eye, there were also small hemorrhages in the medulla, myocardium, and liver, visible under a microscope. The disorders of the blood circulation in these organs were combined with edema: perivascular, pericellular, and perineural edema in the cerebrum, and perivascular edema in the lungs, myocardium, and liver. In addition to this, there were the initial signs of dystrophy in the ganglionic cells of the cerebrum; in the heart, there was proteinic dystrophy, and in the liver, vacuolar dystrophy of the hepatic cells.

In those cases when the animal did not die during the experiment but was killed, no signs of a disorder in the blood circulation were noted by the third day. The hemorrhages and edemata began to dissipate. However, the changes in the organs which occurred as a result of the accelerations continued to develop further. This is particularly evident in the example of the animals which were subjected to accelerations repeated many times. In the organs of such dogs, there were aftereffects of previously intense changes, the quantity and quality of which depended mainly on the magnitude, duration, and frequency of the accelerations they tolerated. Thus, there was an expansion of the ventricles in the cerebrum (all the way to a formation of internal dropsy), dystrophic processes in the ganglionic cells, even leading to death. In the heart, there were hypertrophy of the ventricles, foci of micromyomalacia, and

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thrombosis of the cavities in the right heart and the veins of the epicardium. In the lungs, there were thrombosis of the veins and focal pneumonia, arising against a background of hemorrhages, edema, and atelactases; in some cases, the exudative inflammation becomes productive, leaving sclerotic changes and emphysema. In the liver, there are phenomena which are reminiscent of chronic insufficiency for the right heart (signs of "nutmeg liver") and thrombosis of the veins. In the kidneys, there are productive processes around the conducting arteries and in the glomeruli. In the adrenal glands, there is a disappearance of the lipoids from the protoplasm of the cells in the cortex.

On the basis of the above-described observations, we can assume that the origin of all the morphological changes occurring during the effect of radial acceleration on an organism is an intense disorder in the blood circulation, mainly in the lesser system. As a result of the decompensation of the right ventricle of the heart, the conditions are produced for stasis of the blood in the vena cava, and for its insufficient entry into the system of the left ventricle. This subsequently leads to hypoxia, mainly of the cerebrum and myocardium. These changes are, in all probability, the principal cause of death. Moreover, the disorder in the fluid circulation in the cerebrum, and the stasis in the latter, are of definite significance in the mechanism of death.

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THE EFFECT OF REPEATED ACCELERATION ON THE HISTOLOGICAL STRUCTURE OF THE LIVER

Ye.F. Kotovskiy, T.V. Speranskaya, and A. Yatskovskiy

ABSTRACT: The effect of repeated, transversely-directed accelerations, with values up to 12 units, on the histological structure of the liver was examined in dogs. The repeated accelerations cause the appearance of venous hyperemia, hemorrhaging, embolism and thrombosis of the vessels, vacuolization of the cytoplasm in the hepatic cells, and a decrease in the content of RNA and α-amino acids in these cells. These changes are similar to those which are observed during the effect of single stresses of 8-12 units.

On the basis of the dynamics of development and the degree of the changes observed in the experiment, the authors assume that adaptive reactions which decrease the injurious effect of acceleration are produced during repeated accelerations.

The purpose of our study was to examine the histological structure of the liver after the repeated effect of transverse accelerations on an organism. /308 These problems have not been given due consideration in science. The examinations were conducted on 14 dogs, each of which was subjected to the repeated effect of acceleration in a centrifuge. The accelerations increased in value from 3 to 12 units, and their direction was "chest-back". The intervals between the effects did not exceed 48 hours. The animals were killed with ether, 1 hour, 1, 3, 7, 15, 30, and 60 days after the last stresses in the centrifuge. For the examination, we excised portions of the ventral, central, and dorsal regions of the liver. The sections were stained with hemotoxylin-eosin by the Mallory method, with sudan III by the method of Brashe and Fehlgen, and with α-amino acids.

Within 1 hour after the last effect of an acceleration, there are sharply-outlined foci of old hemorrhages with a rounded or elongated shape in the liver, inside and between the hepatic lobes. The foci of these hemorrhages are strongly infiltrated by leukocytes and, to a lesser degree, by macrophagic elements (Fig. 1). In the focus of a hemorrhage, among the cellular elements of the blood and the connective tissue, we can sometimes see individual dying hepatic cells, with a poorly-stained cytoplasm and pyknotic nuclei, as well as fragments of the walls from destroyed interlobular vessels and bile ducts. Obviously, these hemorrhages, in the

region of which leukocytic and partly macrophagic reactions develop, did not occur during the last effect of an acceleration; they are the result of previous centrifuging of the animals. Fresh hemorrhages are found infrequently. The venous plethora, related to the expansion of the interlobular and sublobular veins, is not very pronounced. As a rule, the intralobular capillaries are not expanded, and in some part of the liver they are even somewhat contracted (possibly because of the swelling of the hepatic cells). /309
The hepatic cells, especially in the central regions of the lobes, are enlarged. Their cytoplasm is light and almost structureless, and they have very noticeable boundaries (the hepatic cells seem to be swollen). The cytoplasm is very weakly stained when we use the methods for detecting the RNA and the α-amino acids. The nuclei of the hepatic cells have a structure which is normal for them.

One day after the effect of the accelerations, old hemorrhages infiltrated with leukocytes and macrophages can be found. The hemorrhages can reach 0.5 mm in diameter. There are no fresh hemorrhages. The collecting, central, and (to a lesser degree) interlobular veins are somewhat expanded, and their lumina are filled with the formed elements of the blood. We obtain the impression that the walls of some interlobular veins and arteries are thickened because of a hypertrophy of the smooth-muscle cells. The possibility that the latter might be hypertrophic can be determined according to the increase of the nuclei - the nuclei have an oval or even round shape. In certain interlobular arteries, the tunica muscularis is hypertrophic on only one side of the vessel wall; on the other side it becomes very small or even disappears. The walls

Fig. 1. Hemorrhage in the Liver, Infiltrated with Leukocytes, 1 Hour After the Effect of the last Acceleration. Staining with Hemotoxylin-Eosin.

of the collecting veins also become thicker because of an increase in the mass of the connective tissue in them. In addition to a moderate venous hyperemia, the interlobular lymph vessels are considerably expanded in a number of cases, and we can find erythrocytes in their lumina. The intralobular capillaries mainly have a normal structure and regular dimensions. It is only in the region of the anterior border of the liver, under the capsule, that the capillaries are expanded and overfilled with blood. In the same regions of the liver (in small areas) there is an insignificant infiltration of the parenchyma with leukocytes along the path of the capillaries. The hepatic cells in the central regions of the hepatic lobes have a light, weakly-stained cytoplasm and clearly-marked boundaries. At the periphery of the lobules, the cytoplasm of the hepatic cells is more intensely stained with dye. In the dorsal regions of the liver, there are small foci with a diameter of about 200 μ, which differ sharply from the remaining hepatic tissue by their white color. These foci consist of swollen partly destroyed hepatic cells, in which the cytoplasm is not stained with dye (as if it were not there). Many cells are stripped of nuclei; in others, they become pyknotic (Fig. 2). In such cells in the cytoplasm, there are no signs of RNA, and almost no α-amino acid. In the remaining hepatic cells, the RNA content remains somewhat decreased, in comparison with the control. This occurs to a great degree in the cells of the central regions of the lobules and (to a lesser degree) at the periphery of the lobules. The quantity of α-amino acid increases in comparison with the preceding period, but it still remains lower than the norm. Desquamation of the epithelium in the wall, as well as adiposis of the cytoplasm in the epithelial cells (in small drops), are observed in certain bile ducts. /310

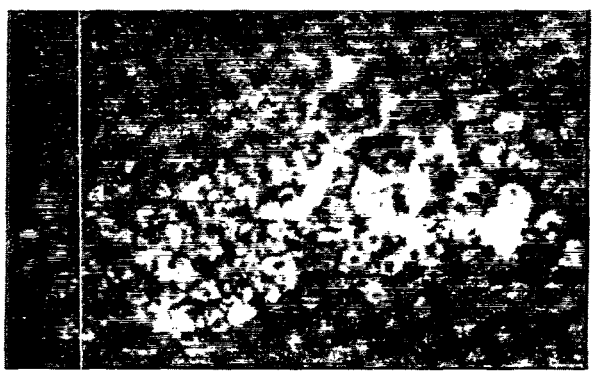

Fig. 2. Extreme Degree of Vacuolization of the Hepatic Cells, One Day After the Effect of the Last Acceleration. Staining with Hematoxylin-Eosin

During the third to seventh days after the effect of the /311
accelerations, the nature of the vascular changes remains almost the same. As before, there are foci of old hemorrhages, which are infiltrated with leukocytes and macrophages. The walls of the interlobular and collecting veins, as well as those of the interlobular arteries, are somewhat hypertrophic in a number of cases. The signs of venous hyperemia are weakly expressed on the third day, while they are lacking entirely on the seventh day. However, the interlobular lymph vessels remain expanded, particularly those which are located along the course of the collecting veins. In the lumina of certain large interlobular and sublobular veins, there are small emboli which consist of several or individual hepatic cells. The emboli are sometimes infiltrated with leukocytes. In one case, the embolus was attached to the wall of the vessel, covering more than half of its lumen (Fig. 3). The interlobular connective tissue surrounding small interlobular and collective veins is rich in leukocytes, among which lymphocytes predominate. In the hepatic /312
cells, we can note more extensive staining of their cytoplasm than in the control, during the detection of RNA and α-amino acids.

The fifteenth day after the effect of the acceleration is characterized by the presence of remnants of those processes whose development we observed during the earlier periods of the experiment. Single foci of old hemorrhages are found. They are intensely infiltrated with leukocytes, among which there are macrophages and some fibroblasts. The walls of certain interlobular arteries and

Fig. 3. Embolus of Hepatic Cells, Infiltrated with Leukocytes, Covering More than Half the Lumen of an Interlobular Vein, Seven Days After the Effect of the Last Acceleration. Staining with Hematoxylin-Eosin.

veins are greatly hypertrophic. The hypertrophy is not uniform in some arteries and veins: the wall of the vessel is much thicker on one side than on the other. The number of muscular elements in the composition of the sphincters which are located in the walls of the sublobular veins increases. As a rule, the sphincters are contracted, so that the sublobular veins in the longitudinal sections have a beaded appearance. The interlobular connective tissue along the course of the sublobular veins is strongly infiltrated with leukocytes, and the perivascular lymph vessels are expanded (their lumina are patent). In one case, in the large branch of the hepatic vein (diameter about 1 mm), there was an organized thrombosis which occupied two-thirds of the lumen of the vessel. The hepatic cells have a structural picture which is normal for them. We can consider that the blood circulation in the liver during this time, despite the presence of the remanent phenomena, is in a condition of complete compensation.

After 30 days, the structural picture of the liver is similar to that described above. A certain hypertrophy of the walls in the interlobular vessels is preserved; however, it is less pronounced than during the preceding period. It is possible that the hypertrophy in the walls of the vessels is a temporary compensatory phenomenon which develops under the conditions of a disordered blood circulation. The infiltration of the interlobular connective tissue with leukocytes is also preserved. There are no changes in the hepatic cells.

Sixty days after the last centrifuging, the liver in one dog has a regular structure, while it is altered in the other dog. In this dog, we note first of all the strong infiltration of the interlobular connective tissue with leukocytes. Among the leukocytes, there are many lymphocytes and eosinophils. Infiltration of segments of the hepatic lobules with leukocytes is found less frequently. The infiltration of the interlobular connective tissue is not identical everywhere. The connective tissue along the small interlobular vessels is strongly infiltrated; along the large vessels, it is much weaker. We obtain the impression that the connective tissue between the hepatic lobules is somewhat expanded. These changes, obviously, do not have a direct relationship with the effect of accelerations on an organism. Thus, repeated accelerations, with intervals of 36-48 hours between effects, cause changes in the /313
system and the hepatic cells in the liver. These changes are similar to those which we observed during previous studies using single accelerations. However, for the repeated effect of accelerations, even for the animals which were killed during the first hour after the last centrifuging, the region of the hemorrhages (as a rule) was infiltrated with leukocytes and macrophages. There were almost no fresh hemorrhages. We must assume that the hemorrhages were caused by the previous rotation of the animals in the centrifuge, and not by the later rotations.

On the basis of these facts, we can assume that repeated

application of accelerations produces adaptative reactions in animals during the experiments and that the reactions last more than two weeks. The adaptive reactions decreased the injurious effect of the last accelerations, whose value reached 12 units.

EFFECT OF MAXIMUM TOLERABLE STRESSES WITH TIME ON THE HISTOSTRUCTURE OF THE LIVER IN MONKEYS

Ye.F. Kotovskiy and T.V. Speranskaya

ABSTRACT: The effect of transverse, maximum tolerable stresses with time, repeated 12 times, on the structure of the liver was examined in monkeys. The authors observed venous hyperemia, destruction of the cells in the blood vessel and hemorrhages as well as thrombosis of the vessels, vacuolization and adiposis of the cytoplasm in the hepatic cells; there was also a decrease in the quantity of RNA and α-amino acids in the hepatic cells. The changes had a recoverable nature.

At the present, in relation to the successful conquest of space, studies dealing with the problem of the effect of flight factors, particularly accelerations, on the histostructure of the tissues and organs are rapidly becoming more numerous. The internal organs of various experimental animals which were subjected to single and repeated effects of transversely-directed stresses (limited in value and time) have been examined. The data obtained indicate that there are regular histostructural and histochemical changes occurring in the vascular system and in the parenchymatous elements of the organs [1-3, 4, 6]. In relation to the liver, it is well known that accelerations can cause deformation of the external shape of the organ, hemorrhages, and vacuolization and adiposis of the hepatic cells [5. 7-9]. /313

The purpose of this study was to examine the effect of maximum tolerable transverse stresses with time (repeated 12 times) on the histostructure of the liver in monkeys (rhesus and baboons). The following characteristics were considered as the criterion for tolerance: prolonged suppression or arrest of respiration, significant tachycardia or disorders in the function of automatism, excitability and conductivity of the cardiac muscle. The time for tolerance, in relation to the individual features of the animals, varied from 1 to 5 minutes.

We examined 13 animals in all. The monkeys were killed with ether 30 minutes, 1 hour, and 1 and 3 days after the effect of the accelerations. For the examination, we excised portions of the ventral, central, and dorsal regions of the liver. Paraffin and celloidin sections, as well as sections prepared on a freezing microtome, were stained with hemotoxylin-eosin (by the Mallory method) and with sudan III (by the method of Brashe and Fehlgen). /314

RESULTS

Thirty minutes after the effect of the accelerations, there are signs of venous and (to a lesser degree) capillary hyperemia in the liver. These vessels are greatly expanded and filled with formed elements of the blood. These changes are most significantly pronounced in the dorsal regions of the liver, in the central and collecting veins. In many central, collecting, and interlobular veins, we can observe a swelling of the nuclei, fogging, and vacuolization of the protoplasm in the endothelial cells, and desquamation of some of the latter around the lumina of the vessels. In addition, the walls of the vessels show loosening of the connective tissue and rupture of individual collagenic fibers in it. In a number of cases, the walls of the vessels and the connective tissue surrounding them are infiltrated with leukocytes to varying degrees. In the lumina of the vessels, there are sometimes small, parietal, leukocytic thrombi. Small (punctate) hemorrhages, caused by rupture of the wall of the vessel or having a diapedesic nature, are very rare (Fig. 1). The first type of hemorrhage is usually found in the central regions of the organ, while the second type of hemorrhages is found more frequently in the dorsal regions of the liver. As for the hepatic cells, there are signs of vacuolization of their protoplasm. This process usually has a focal nature, mainly affecting the cells in the central regions of the hepatic lobules. It is not uniform in the various lobules. Sometimes segments are found to contain hepatic cells in which vacuolization has reached an extreme degree: large vacuoles almost completely fill the hepatic cells. However, there are no signs of vacuolization in most of the hepatic cells. The quantity of RNA and α-amino acids

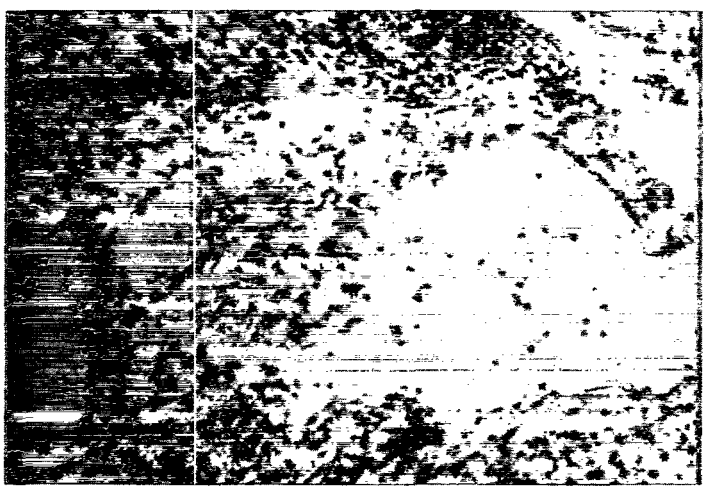

Fig. 1. Hemorrhage as a Result of a Rupture in the Wall of a Collecting Vein, One Hour After Rotation in a Centrifuge.

in the protoplasm of strongly vacuolized cells decreases, while it remains within the limits of the norm or even increases slightly in the remaining cells. In the latter case, this affects the amount of α-amino acids to a great degree, and the amount of RNA to a lesser degree. It is very probable that some hepatic cells undergo complete destruction. This is indicated by the appearance of single or small groups of hepatic cells in the lumina of large veins, where they form various types of emboli. Apparently, their origin is to be found in ruptures of the walls of the vessels and the destruction of hepatic cells at the site of a hemorrhage.

One hour after rotations in a centrifuge, the signs of hyperemia are still preserved. Moreover, there is an expansion of the interlobular lymph vessels, as well as the appearance of Disse spaces in a large number of cases, located among the liver cells. In the lumina of the veins, there are individual hepatic cells, desquamated cells of the endothelium, and single parietal thrombi. The walls of the vessels and the connective tissue surrounding them are edematous. We can sometimes observe small hemorrhages, caused by fresh formed elements of the blood, around the vessels. The processes of vacuolization of the hepatic cells are more strongly pronounced, while the quantity of such cells is greater in comparison with that for the previous period. In the protoplasm of the hepatic cells and in the epithelial cells of the bile ducts, there are small drops of fat. The intensity of the stain in the protoplasm of the hepatic cells for RNA and α-amino acids is somewhat less than in the preparations of the preceding period, and in some cells it is even lower than in the control. After one day, the signs of hyperemia decrease significantly. However, the processes of migration of the leukocytes and their infiltration of the walls of the vessels and the surrounding connective tissue (as well as the hemorrhagic foci) are more strongly pronounced. Sometimes small emboli, consisting of degenerate hepatic cells and infiltrated with leukocytes, are found in the lumina of the vessels. There is vacuolization and adiposis (in the form of small drops) of certain hepatic cells, and cells in the epithelium of the bile ducts (Fig. 2). The intensity of the stain in the protoplasm of the hepatic cells for RNA and α-amino acids is somewhat less than in the controls. On the third day after the effect of the stresses, the signs of plethora, which were so characteristic for the earlier periods of the experiment, disappear in most of the vessels. However, certain vessels, and mainly the interlobular and central veins, remain expanded. Obviously, this is the result of a loss in the tonus of their walls. The perivascular connective tissue, and sometimes the walls of the vessels, are edematous in places and infiltrated with leukocytes. In certain vessels, we can detect small parietal thrombi and emboli from hepatic cells (Fig. 3). The old hemorrhages are dispersed because of the macrophagic elements which are formed from Kupfer cells. Fresh perivascular hemorrhages of a diapedesic nature are found infrequently in some animals. Signs of vacuolization and adiposis of the hepatic cells are noted only in cells located in the central regions of the liver lobules. The intensity

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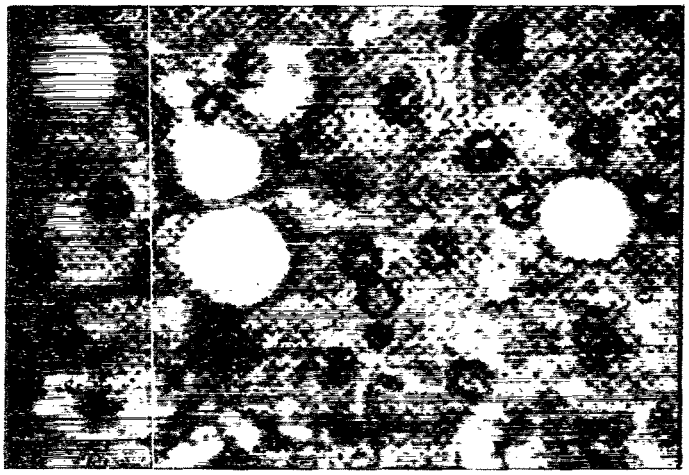

Fig. 2. Vacuolization of the Protoplasm of Hepatic Cells, One Day After Rotation in a Centrifuge.

Fig. 3. Embolus in the Lumen of a Collecting Vein, Three Days After Rotation in a Centrifuge.

of the stain in the cytoplasm of the hepatic cells for α-amino acids, corresponds to that in the control for two animals, while it is somewhat greater for three others. The degree of staining in /317
hepatic cells for RNA remains at a lower level for all the animals than in the control. These changes mainly affect the hepatic cells which are in the center of the lobes, while the hepatic cells at the periphery of the lobes keep roughly the same amount of nucleic acid as the control.

Thus, the materials obtained show that accelerations which are repeated 12 times and are the maximum tolerable (1-5 min), cause changes of a principally vascular nature in the liver. These changes are expressed by the appearance of venous, stagnant hyperemia which begins in the system of hepatic veins. The signs of hyperemia become complicated because of the dystrophic processes in the elements of the vessel walls, the edema of the surrounding connective tissue, and the formation of small (punctate) hemorrhages. The signs of hyperemia are most pronounced in the dorsal regions of the liver, and the hemorrhages which are formed by the rupture of vascular walls are found most frequently in the central regions of the organ. Obviously, these facts can be explained by the concept that difficulty in blood flow into the system of hepatic veins and a simultaneous redistribution of the blood in the direction of the acceleration cause the most significant blood pressure increases to occur in the vessels of the central regions of the liver. The destructive changes on the part of the endothelium in the vessels /318
are obviously caused by a condition of temporary hypoxia, and are the cause of the formation of thrombi, while the ruptures of the vessels and the hemorrhages cause the appearance of the emboli which consist of hepatic cells. The processes of vacuolization of the protoplasm in the hepatic cells, which reflect disorders in the water exchange in the liver (according to the data in the literature), are typical for the condition of hemostasis in the system of the lower vena cava. We can also assume that during accelerations the protein metabolism of the liver also suffers to some degree, as indicated by the changes in the percentage of RNA and α-amino acids in the hepatic cells.

In conclusion, we should note that the changes were of the same type in all the animals, but they increased with an increase in the time of the animals' individual tolerance to acceleration.

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THE EFFECT OF PROLONGED TRANSVERSELY-DIRECTED RADIAL ACCELERATIONS ON THE MOTOR ACTIVITY OF THE UPPER PART OF THE GASTROINTESTINAL TRACT IN DOGS

A.P. Mukhina and V.Ye. Potkin

ABSTRACT: The data from studies of the periodic motor activity of the stomach, associated with hunger, as well as of the duodenum, are presented in relation to the effect of transversely-directed radial accelerations (back-chest) of 8 g for 3 min.

The examinations conducted showed that singly-imposed accelerations cause a change in the relationship between the periods of work and rest in the motor activity of the stomach, and of the duodenum in particular, with after effects persisting for about three weeks. The rhythmic and peristaltic activity of these regions of the digestive apparatus remained unchanged during a two-month period of observation after the effect of the accelerations.

The information in the literature concerning the effect of /318
on the function of the digestive system is limited [1-4,6,7]. The data which are available [3,4] concerning the motor activity of the gastrointestinal tract involve studies which were conducted on human subjects during the effect of longitudinally-directed radial accelerations (pelvis-head) of 5 g, lasting 30 sec. In this case, the author did not note any significant changes in the periodic contrac- /319
tions of the stomach. Nevertheless, an examination of the periodic motor activity of the upper region, associated with humger, is of great interest, since its role in the system of the digestive apparatus has great significance. Moreover, we can assume that the stresses we imposed (most intense in value and duration) can cause changes in the motor activity of the digestive apparatus.

The purpose of this study was to conduct examinations on the periodic motor activity (associated with hunger) of the stomach and the duodenum during the effect of transversely-directed radial accelerations (back-chest) of 8 g, lasting for 3 minutes. According to the data of Slapp [8], such a characteristic effect of the accelerations can occur when a space craft has exceeded escape velocity by a factor of 2.

The study was conducted on dogs with gastric fistulae, according to Basov. The examinations were accomplished by the method of

parallel two-balloon recordings. For the indices of motor function, we determined the length of the periods of function and rest, the time for a complete cycle of periodic motor activity of the stomach and the duodenum, and the frequency of the rhythmic activity for the regions being examined.

After the background data for the motor periodic activity associated with hunger had been determined, the animals were subjected to the effect of transversely-directed radial accelerations of 8 g for 3 min, in a centrifuge with a radius of 4.2 m. The rate of increase for the stress was 0.2 g/sec. The experiments were conducted 18-20 hours after the animals had been fed.

After the effect of the accelerations, we noted significant divergence in the motor periodic activity associated with hunger, in the regions we were examining. On opening the gastric fistulae, we removed a large quantity of bile with mucus. The insertion of the balloon into the duodenum through the gastric fistula became difficult on the first day after the effect.

Figure 1 shows the kymograms of the parallel recording for the periodic activity of the stomach and the duodenum, before and after the effect of the accelerations. The data were obtained for the dog Seryy.

As we can see from the figure, the periods of rest for the stomach, before the effect of the accelerations, are roughly 60-70 min, and the periods of function are 18-20 min; for the duodenum, they are 62-75 and 21-22 min, respectively. The time for a complete cycle of the periodic motor activity of the stomach was 75-90 min; for the duodenum, it was 80-95 min.

Two hours after the effect, we observed a continuous motor activity of the stomach and the duodenum (Fig 1B), a type of acid contraction lasting throughout the entire experiment (6.5 hours).

On the fourth day after the effect, we noted shortening of /320
the "rest" periods for the stomach; the duration became 20-23 min, instead of the 60-70 min during the period of the background examinations. The length of time for rest of the duodenum was 18-20 min. The time for a complete cycle of periodic motor activity also changed correspondingly. Thus, for the stomach, the time for a complete cycle of periodic motor activity was 40-42 min; for the duodenum, it was 42-45 min (Fig. 1C).

Toward the end of the third week (Fig. 1D), the periodic motor activity associated with hunger was recovered.

For another dog (Shustrik), we obtained somewhat different data. The periods of rest for the stomach in this dog were much shorter (roughly 36-40 min). The periods of function were the same as for Seryy, i.e., 20-25 min. The complete cycle of periodic activity

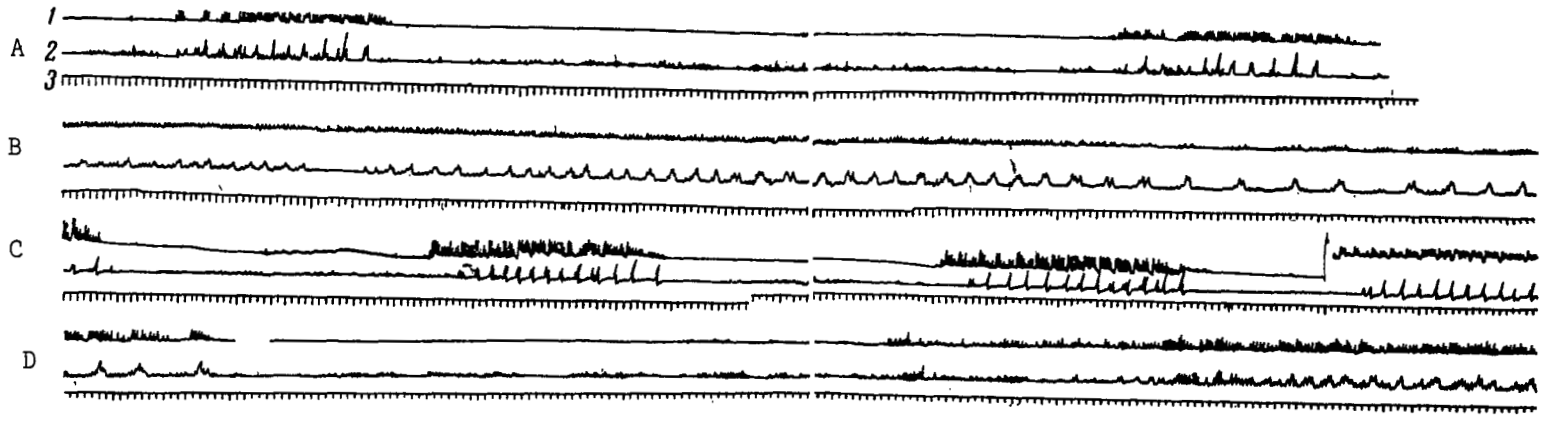

Fig. 1. Periodic Motor Activity (Associated with Hunger) of the Stomach (2) and the Duodenum (1) for the Dog Seryy. (A) Background; (B) Two Hours After the Effect of the Accelerations; (C) On the Fourth Day; (D) At the End of the Third Week; (3) Time, sec.

lasted 55-65 min, on the average. The time for the rest period of the duodenum was equal to 42-45 min, while the period for function was 24-26 min. The complete cycle of periodic activity lasted roughtly 65-70 min.

Two hours after the effect, the recordings for this dog showed an increase in the period of rest for the stomach to 75 min, while the period of function increased up to 50 min. The period of rest for the duodenum at the beginning of the experiment lasted 18 min, while the period of function lasted more than 100 min. After this, a period of rest in the activity of the duodenum did not appear. Thus, the time for the first complete cycle of periodic motor activity of the stomach was equal to 125 min. During the remainder of the experiment, there was a continuous motor activity of the stomach in the form of acid contractions. The appearance of continuous motor function of the stomach and the duodenum observed on /321
the day of the effect of the accelerations was preserved on the fourth day of the after effects. Following this, there was a period of normalization; aroung the end of the third week, just as for Seryy, there was a beginning of recovery of the periodic motor activity, associated with hunger, for these regions of the gastrointestinal tract.

The rhythmic and peristalic activity of these regions in the digestive apparatus remained unchanged throughout the entire two-month period of observations after the effect of acceleration.

The examinations conducted showed that the single effect of prolonged transversely-directed radial accelerations on the dogs causes significant changes on the part of the motor periodic activity associated with hunger for the stomach and duodenum. These changes are expressed by changes in the periods of function and rest of the stomach (particularly the duodenum), with after effects lasting about three weeks.

The changes noted in the periodic motor activity of the stomach and duodenum can be used to analyze the pathology of the gastrointestinal tract in human subjects who are subjected to accelerations affecting their activity.

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THE PROBLEM OF THE ROLE OF THE SMALL INTESTINE IN THE REGULATION OF THE LEVEL OF CHOLESTEROL IN THE BLOOD, DURING THE EFFECT OF TRANSVERSELY-DIRECTED RADIAL ACCELERATIONS

M.S. Martsevich and V.Ye. Potkin

ABSTRACT: The change in the cholesterol content in the blood and in the intestinal juice was examined after the effect of radial accelerations in dogs with isolated sections of the small intestine. It was established that the effect of transversely-directed radial accelerations causes an increase in the cholesterol content in the blood, with a simultaneous decrease in its content in the intestinal juice. In the case of an increase of the cholesterol content in the intestinal juice after the accelerations, there was no hypercholesterinemia observed.

The facts presented show that the functional condition of the small intestine has definite significance in the development of hypercholesterinemia during the effect of accelerations on an organism.

Recently, information has appeared in the literature which in- /322
dicates that the cholesterol in the blood increases in people who are subjected to the effects of extreme stimuli. In particular, a number of authors [1,2,4,6,7] have observed an increase in the concentration of cholesterol in the blood during the first 2-3 days after flights in aircraft.

Similar results were obtained in examining the astronauts of the first and second group flights, in whom an increase of the cholesterol content in the blood was observed for the following two weeks [5,9].

A large amount of data has recently been obtained on the significance of the functional condition of the digestive system in the development of disorders in the lipoid and, in particular, the cholesterol exchange [8,11,12].

In relation to this, we attempted to examine the appearance of a relationship between the cholesterol content in the blood (according to the method of Engelhardt and Smirnova in the Zamychkina modification), and its secretion in the intestinal juice, during the effect of transversely-directed radial accelerations on an organism.

The study was conducted on dogs, with loops of the upper part of the small intestine isolated according to Thiry.

After establishing the background, we subjected the animals to a single effect of transversely-directed acceleration (back-chest) of 8 g for 3 min. The accelerations were produced in a centrifuge with a radius of 4.2 m. The rate of increase for the accelerations was 0.2 units/sec.

As a result of the studies conducted, we established that the /323
effect of radial acceleration causes a regular increase of the cholesterol concentration in the blood, and a simultaneous decrease of the cholesterol concentration in the intestinal juice on the day of the experiment (Fig. 1).

As we can see from the figure, the cholesterol content in the blood increased more or less (by 10-70 mg%) in all cases following the acceleration. The cholesterol content in the intestinal juice, on the other hand, decreased (by 5-20 mg%).

A statistical analysis of the data revealed a change in the direct correlation between the cholesterol contents in the intestinal juice and in the blood before the acceleration, with a reverse correlation after the acceleration.

Having established the relationship between the changes in the cholesterol content in the blood after the acceleration and its concentration in the intestinal juice, we found it interesting to

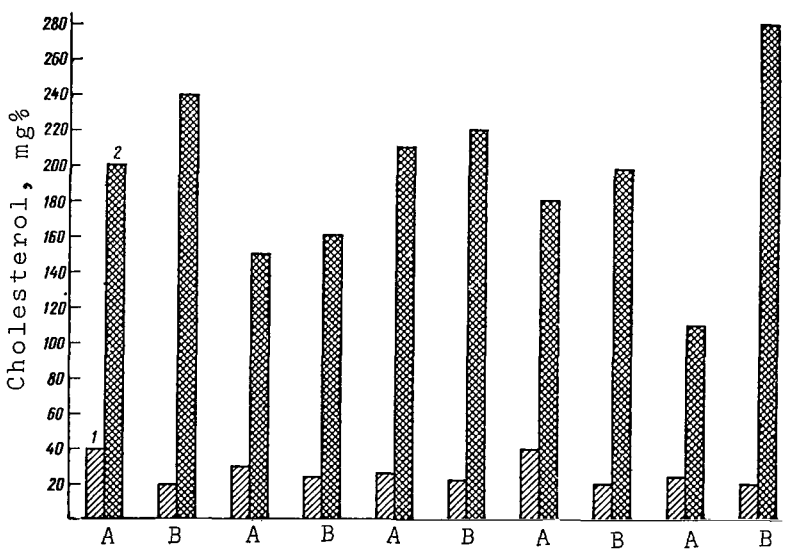

Fig. 1. Cholesterol Content in the Blood (2) and in the Intestinal Juice (1) Before (A) and After (B) a Single Acceleration.

make prolonged observations of the disorders. For this purpose, we studied the cholesterol concentration in the blood and the intestinal juice for a number of dogs, for 2 months after the accelerations.

Figure 2 (A) and (B), shows the data obtained for the dogs Yunets and Valet. In the dog Valet, as for most of the animals, the cholesterol in the blood was increased after the stresses; for the following two months, it remained at a higher level relative to the background (Fig. 2). If the norm for a given dog allowed the cholesterol concentration in the blood to vary from 115 to 160 mg%, after the effects it varied from 170 to 180 mg%. /324

The cholesterol content in the intestinal juice varied from 20 to 40 mg% before the stresses, and from 25 to 55 mg% after them. In the intestinal juice, the cholesterol content was within the limits for the background in the majority of the experiments. In the dog, Yunets (in contrast to the others), the effect did not cause any significant increase in the cholesterol concentration in the blood for the entire period of the observations. Before the stresses, the cholesterol concentration in the blood varied from 130 to 190 mg%; after the stresses and for the following two months, it varied from 135 to 160 mg%.

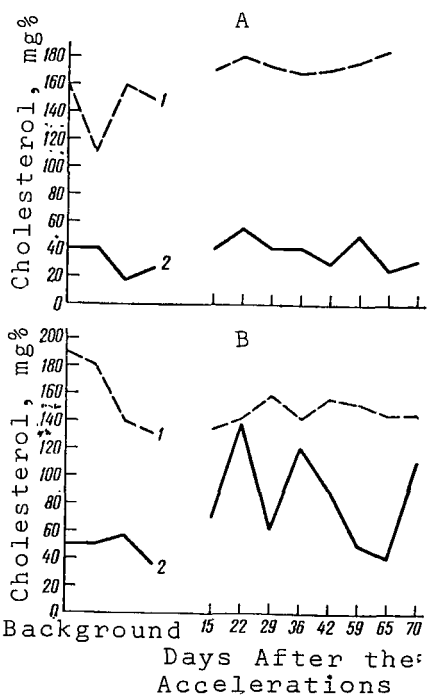

Fig. 2. Cholesterol Content in the Blood (1) and in the Intestinal Juice (2), in the Dynamics Following Single Radial Accelerations of 8 g for 3 min, in the Dogs Valet (A) and Yunets (B).

At the same time, the cholesterol content in the intestinal juice increased. As compared to a norm of 35-55 mg%, its level varied between 40 and 140 mg% after the stresses. Moreover, in most of the experiments, the cholesterol content in the intestinal juice was much higher than the background value.

Therefore, the experimental data we obtained show that the effect of transversely-directed radial accelerations causes an increase in the cholesterol concentration in the blood, with a simultaneous decrease in its content in the intestinal juice. In the case of an increase of the choles-

terol content in the intestinal juice after the effect of the accelerations, no hyper-cholesterinemia was observed.

The facts we have presented show that the functional condition of the small intestine has definite significance in the development of hypercholesterinemia during the effect of acceleration on an organism.

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THE ROLE OF THE CENTRAL NERVOUS SYSTEM IN THE REGULATION OF THE SECRETORY ACTIVITY OF THE SMALL INTESTINE, AFTER THE EFFECT OF PROLONGED TRANSVERSE ACCELERATIONS

V.Ye. Potkin

ABSTRACT: The materials from a study of the secretory activity of the small intestine after the effect of prolonged transverse accelerations (8 g for 3 min) are presented in relation to dogs with isolated normal and denervated intestinal sections.

The differences in the secretion of the intestinal juice and the enzymes of enteropeptidase, alkaline phosphatase, amylase, and lysozyme by different sections are shown. The important role of the central nervous system in the regulation of the secretory activity of the small intestine is established.

The study of the role of the central nervous system in the function of various organs and systems during the effect of extreme factors on an organism has an important place in the research of space and aviation physiology. /325

This study examines the role of the central nervous system in the secretory activity of the small intestine after the effect of radial accelerations.

For this purpose, we used dogs with denervated intestinal sections. In one dog (Damka), the intestinal section was denervated according to the method of V. N. Shamov (1926); in two others (Nora and Sivyy), this was done by the method of L.S. Fomina (1955). Since the latter two dogs also had fistulae isolated according to Thiry, in addition to the denervated intestinal sections, the studies of the secretory activity of all the sections were conducted in a parallel manner. /326

The examinations began three or four weeks after denervation. We determined the secretory activity according to the quantity of intestinal juice and the activity of these enzymes: enteropeptidase, alkaline phosphatase, amylase, and lysozyme. We sampled the intestinal juice both during periodic secretion and during secretion in response to mechanical stimulation.

After the background was established by these characteristics, the animals were subjected to the effect of transverse acceleration of 8 g for 3 min, with a rate of increase in the stress of 0.2 units/sec.

Despite the various locations of the intestinal sections (in Damka, a section was implanted under the skin, while in Nora and Sivyy the sections were in the peritoneal cavity), the results obtained from the studies were similar for all the dogs (Figures 1 and 2).

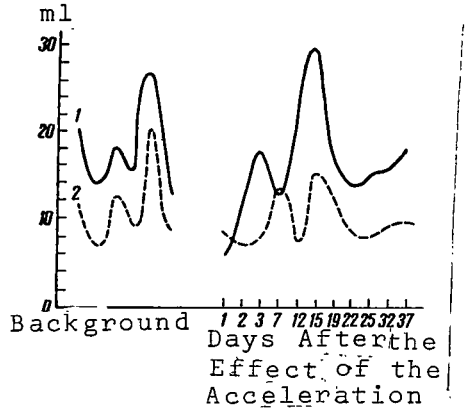

Fig. 1.

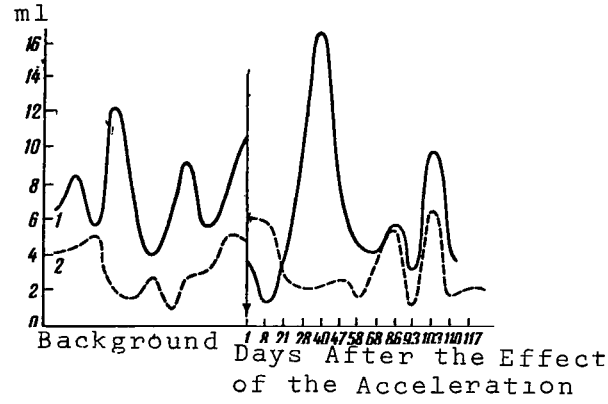

Fig. 2.

Fig. 1. Secretion of Intestinal Juice in Response to Mechanical Stimulation, from Denervated (2) and Normal (1) Sections, Before and After the Effect of Prolonged Transverse Accelerations for the Dog Sivyy.

Fig. 2. Secretion of Intestinal Juice from Denervated (2) and Normal (1) Intestinal Sections, During their Periodic Activity Before and After the Effect of Prolonged Transverse Accelerations, in the Dog Nora.

As we can see from the figures, there was much less excretion of intestinal juice from the denervated segment. The same regularity was also observed in the activity of the enzymes, which agrees with the data of L.S. Fomina (1956). After the stress, the activity of the intestinal enzymes in the juice from the denervated intestinal section remained on a much lower level than the activity of the enzymes in the juice from the intestinal section which was linked with the extramural nervous system. The only change occurred in the secretion of the intestinal juice after the stress. Thus, while the quantity of juice obtained from a denervated intestinal section continued to show no particular change, the quantity of juice from a section isolated according to Thiry decreased sharply. This indicates that the changes in the secretory activity of the small intestine, affected by the radial accelerations, occur indirectly through the central nervous system.

During the period of the after effects, the intestinal juice of a denervated section showed an increase in the activity of the alkaline phosphatase and amylase, while the activity of the lysozyme decreased; the duration of the changes observed was the same

as for the juice from a normal intestinal section. The activity of the enteropeptidase was not examined systematically; therefore, it did not appear possible to determine the dynamics of its changes. We can only say that its activity was at a much lower level than in the juice from a regular section (Table 1). /327

A comparison of the studies, after a statistical analysis, also showed that the changes in the secretory activity of both intestinal sections had the same direction.

TABLE 1. SECRETION OF INTESTINAL JUICE AND ENZYMES FROM DENERVATED AND NORMAL INTESTINAL SECTIONS, BEFORE AND AFTER THE EFFECT OF PROLONGED TRANSVERSE ACCELERATIONS OF 8 g FOR 3 MIN, FOR THE DOG SIVYY.
(Averaged Data)

Indices	Before Acceleration	After Acceleration	Change, %	p
Amount of Intestinal Juice, ml	17,4±2,08	13,5±1,7	—24,4	<0,1
	11,1±2,1	9,5±0,88	—14,4	<0,1
Alkaline Phosphatase, arbitrary units/ml	7600±2040	32300±12400	+320	<0,05
	6610±2400	8200±3050	+24	<0,1
Amylase, arbitrary units/ml	14,3±3,6	35,7±9,7	+149	<0,05
	12,0±7,3	53,0±15,4	+342	>0,05
Lysozyme, arbitrary units/ml	691±120	247±104	—64,2	>0,02
	379±88,5	226±95	—40	<0,1

NOTE: The indices for secretion from a normal intestinal section are shown above the line; those from a denervated section are shown below the line.

Therefore, the results we obtained show that, after the effect of transverse accelerations, the quantity of the juice decreases in the denervated intestinal sections, the activity of the enteropeptidase, amylase, and alkaline phosphatase increases, and the activity of the lysozyme decreases. The unidirectionality of the changes shows the neurohumoral regulation of the secretory activity in the small intestine, however, the lack of change in the quantity of the intestinal juice obtained from the denervated section of the intestine on the first day after the accelerations, and the significantly lower level of the changes during the period of the aftereffects in comparison with the secretion of the juice and enzymes from the intestinal section with a preserved nerve link, show the important role of the central nervous system in the regulation of the secretory activity of the small intestine. /328

WEIGHTLESSNESS AND CELL DIVISION IN MICROSPORES OF TRADESCANTIA PALUDOSA

N. L. Delone

ABSTRACT: Grafts of Tradescantia paludosa, with racemes in special "bio-cartridges", were placed in the cabins of the "Vostok-3", "Vostok-4", "Vostok-5", "Vostok'6", and "Voskhod" spacecraft.

Five types of disorders of mitosis in the microspores of the Tradescantia, related to the effect of weightlessness, were found.

Factors which are characteristic of space, as well as factors related to the dynamics of space flight (primarily weightlessness) affect living cells during space flight. /328

In our experiments aboard the "Vostok-3", "Vostok-4", "Vostok-5", "Vostok-6", and Voskhod" spacecraft with microspores of Tradescantia paludosa, we discovered a number of disorders in cell division. However, it remains to be explained whether or not the duration of the flight affects the number of disorders which occur. And if this effect does occur, what factor of space flight causes these disorders?

OBJECT AND METHODS

The object of the studies (microspores of Tradescantia paludosa, Sachs strain No. 5), the method of cytological preparation, and the apparatus of the "bio-cartridges" were described in detail in our preceding articles [1-3]. The essence of the method in the study of the microspores of Tradescantia is the following: if we know the time of the effect of any factor on the object and the time of fixation of the anthers, we can establish the phase of mitosis at which the effect took place, with a sufficient degree of accuracy. At 20°, the entire cycle of cell division in the first postmeiotic mitosis occurs in 10 days, while at 30° it occurs in 7 days. Thus, the time for the passing of each orbit, beginning with the interphase, can be calculated. Therefore, the accuracy of determining the length of the mitotic phases depends on the accuracy of the data on the changes in temperature during the experiment. Having analyzed the cytological preparations with the /329 microspores of spider-wort, we can use a microscope to find any visible changes and determine which factor, at which phase of mitosis, led to the given disorder.

RESULTS

We found 5 types of disorders in mitosis (Figures 1 and 2). In normal mitosis, the nucleus is located at the center of the cell

during the early interphase, and then moves toward a corner. In the middle prophase, it returns to the center. The metaphasal layer remains parallel to the thickened wall of the microspore. The separation of the chromosomes in the telophase and the nuclei in the binuclear pollen is definitely secured, and the generative nucleus is located around the thickened wall. The morphological pictures of the disorders we discovered are the following:

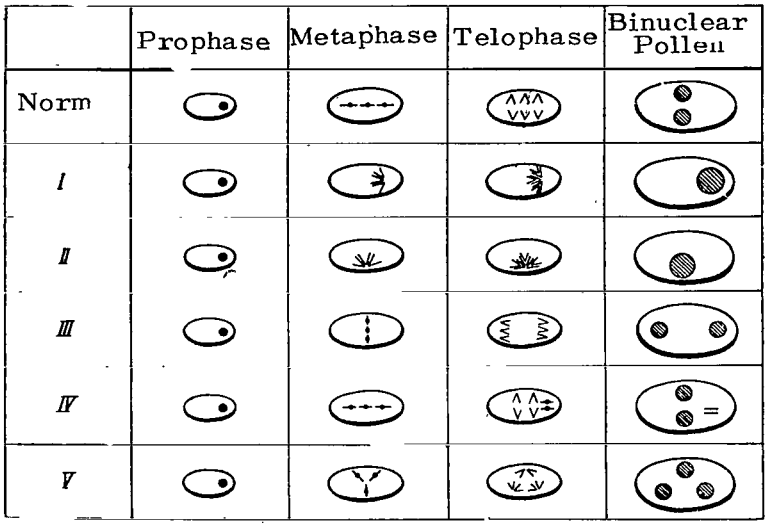

Fig. 1. Five Types of Disorders in the Mechanism of Mitosis in Microspores of Spiderwort.

Type I. The nucleus remains near the rim of the cell, and does not move toward the center. However, the chromosomes form individual metaphasal bodies and split, as in the anaphase; they do not become separated, but remain attached to centromere segments. A mononuclear cell, instead of binuclear pollen, is formed.

Type II. The nucleus moves forward toward the center of the cell in the prophase, but in the metaphase all the chromosomes seem to be joined to centromere segments and form a "rosette". The chromosomes split up, as in the anaphase and telophase, but they are not separated. Then, as in Type I, a mononuclear cell is formed, instead of a binuclear pollen. /330

Type III. The direction of the axis of the spindle changes. The chromosomes in the metaphase and telophase, and the nuclei in the binuclear pollen, are located in a different plane than in the norm.

Type IV. There is no separation of individual chromosomes.

Type V. Tri-polar and tetra-polar mitoses occur, leading to

to the formation of tri-and tetra-nuclear cells.

In preparing the preparations, there may be artefacts which are similar to Type III; they should be kept in mind when analyzing the materials. However, Types I, II, IV, and V of the disorders do not appear in this case.

The flights of all of the spacecraft led to the appearance of disorders in the mechanism of mitosis (Tables 1 to 5, Figures 3 and 4). For a more detailed analysis, the astronauts performed fixation of the materials at various stages of flight: P.R. Popovich, after 56 hours; V.F. Bykovskiy, 1, 5, 76, and 120 hours after launching; B.B. Yegorov, 1 hour and 30 minutes before landing. After the landing, the materials were also fixed at various intervals.

The degree of reliability for the differences in the data between the experimental groups from the craft "Vostok-5", which were fixed at various times, is the following: between the first fixation by V.F. Bykovskiy (1.5 hours after launching) and the second (after 76 hours), it is $R = 2.5$; between the first fixation and the fourth (3.5 hours after landing), it is $R = 10.5$. The degree of reliability for the difference in the data between the experimental groups from the craft "Voskhod-1" is the following: for fixation 2 hours and 15 min (and 48 hours) after landing, it is $R = 4.5$; for fixation 24 (and 48) hours after landing, it is $R = 4.5$; for fixation 48 (and 120) hours after landing, $R = 6.2$.

It was established that disorders of Type III occur earliest, while those of Types II and V occur last.

DISCUSSION

We did not collect enough materials to answer the question of the nature of the causes for the disorders in the mitosis that occurred: whether there were directional bodies and centromeres which participated actively in the mitosis, or whether the disorders occurred as a secondary effect. Types I and II could have occurred during non-separation of a directional body; Type V, during extraneous division of the directional body; Type IV, during injury of a centromere. Nevertheless, it is possible that all the structures were preserved as a whole, while the particular conditions of the flight caused a disorder in their function.

The events occurring in relation to the reoriented spindle obviously could appear even after the spindle was first established correctly. A confirmation of this assumption is, for example, the significant number of incorrectly-arranged nuclei in the binuclear pollen, even 1.5 hours after the launching of the "Vostok-5". Not all the recorded mitotic disorders have the character of genetic changes. Thus, the most frequently found Type III should lead to a normal formation of gametes. However, Types I and II lead to the formation of polyploid cells, and Types IV and V lead to aneu-

Fig. 2. Microspores of Spiderwort Before (1-3) and After a Space Flight (4-8). (1) Metaphase; (2) Telophase; (3) Binuclear Pollen; (4) Binuclear Pollen with Center-Oriented Nuclei; (5) Chromosomes Joined with Centromeres at a Corner of the Cell; (6) "Rosette" of Chromosomes; (7) Remaining Chromosome; (8) Incorrect Arrangement of the Chromosomes.

TABLE 1. NUMBER OF CELLS WITH MITOTIC DISORDERS IN THE MICROSPORES OF TRADESCANTIA PALUDOSA, OCCURRING UNDER THE INFLUENCE OF FACTORS OF SPACE FLIGHT ABOARD THE "VOSTOK-3" AND "VOSTOK-4" SPACECRAFT. (ANALYSIS OF ANAPHASES AND TELOPHASES)

Time of Fixation of the Materials	Phases of Mitosis Affected by the Factors	No. of Cells	No. of disorders		Types of disorders							
					I		II		III		IV	
			abs.	in % ± m	abs	%	abs	%	abs	%	abs	%
"Vostok-4" 56 Hours After Launching	Late Interphase; Early, Middle, and Late Prophase; Metaphase; Middle and Late Interphase Early Prophase	712	15	2,11±0,54	3	0,42	6	0,35	4	0,56	2	0,28
" Vostok - 3", 18 hrs after landing		401	4	0,99±0,50	1	0,25	2	0,49	1	0,25	—	—
"Vostok-4" 48 hrs after landing	Middle Interphase	33	2	2,40±1,68	—	—	—	—	1	1,20	1	1,20
Control in Moscow		1000	—	—	—	—	—	—	—	—	—	—

TABLE 2. NUMBER OF CELLS WITH MITOTIC DISORDERS IN THE MICROSPORES OF TRADESCANTIA PALUDOSA, OCCURRING UNDER THE INFLUENCE OF FACTORS OF SPACE FLIGHT ABOARD THE "VOSTOK-3" AND "VOSTOK-4" SPACECRAFT. (ANALYSIS OF BINUCLEAR POLLEN)

Time of fixation of the materials	Phases of mitosis affected by the factors	no. of cells	Types of disorders			
			V		III	
			abs	in % ± m	abs	in % ± m
"Vostok-4" 56 hrs after launching.	Binuclear pollen	500	1	0,2±0,20	11	2,2±0,65
"Vostok-3" 18 hrs after landing.	Late interphase, Early, Middle, and Late Prophase	500	4	0,8±0,39	13	2,6±0,71
"Vostok-4" 48 hrs. after landing	Middle and Late interpnase	500	2	0,4±0,28	7	1,4±0,53
Control at the Cosmodrome	—	500	—		2	0,4±0,28
Control in Moscow	—	500	—		1	0,2±0,20

TABLE 3. NUMBER OF CELLS WITH MITOTIC DISORDERS IN THE MICROSPORES OF TRADESCANTIA PALUDOSA, OCCURRING UNDER THE EFFECT OF FACTORS OF SPACE FLIGHT ABOARD THE "VOSTOK-5" AND "VOSTOK-6" SPACECRAFT. (ANALYSIS OF ANAPHASES AND TELOPHASES)

Time of fixation of the materials	Phases of Mitosis affected by the factors	No. of cells	No. of disorders		Types of disorders							
			abs	% ± m	I		II		III		IV	
					abs	%	abs	%	abs	%	abs	%
"Vostok-5", 1.5 hrs after launching.	Late Prophase Metaphase	1231	6	0,49 ± 0,20	1	0,08	1	0,08	4	0,33	—	—
"Vostok-5" 76 hrs. after launching.	Late Interphase, Early, Middle, and Late Prophase, Metaphase	401	10	2,50 ± 0,80	2	0,50	3	0,75	4	1,00	1	0,25
"Vostok-5" 120 hrs after launching	Early, Middle, and Late Interphase, Prophase, Metaphase	1032	32	3,10 ± 0,17	7	0,68	11	1,07	13	1,26	1	0,09
"Vostok-5" 3.5 hrs after landing	Early, Middle, and Late Interphase, Early and Middle Prophase	1845	54	2,92 ± 0,12	14	0,76	17	0,92	20	1,08	3	0,16
"Vostok-6" 4.5 hrs after landing	Middle and Late Interphase, Early and Middle Prophase	2249	62	2,75 ± 0,10	16	0,65	21	0,93	23	1,08	2	0,09
Control at the Cosmodrome	—	1000	—	—	—	—	—	—	—	—	—	—

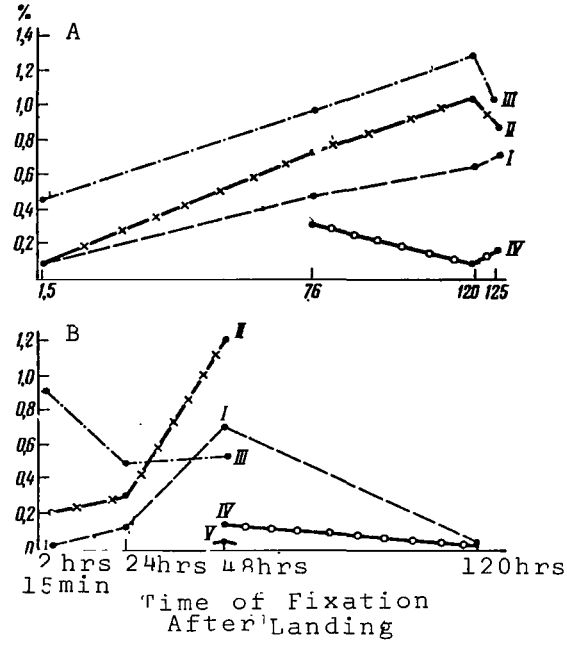

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Fig. 3. Various Types of Mitotic Disorders (in %) Occurring in Cells during Flight Aboard the "Vostok-5" (A) and "Voskhod" (B). The Numbers Indicate the Types of Disorders.

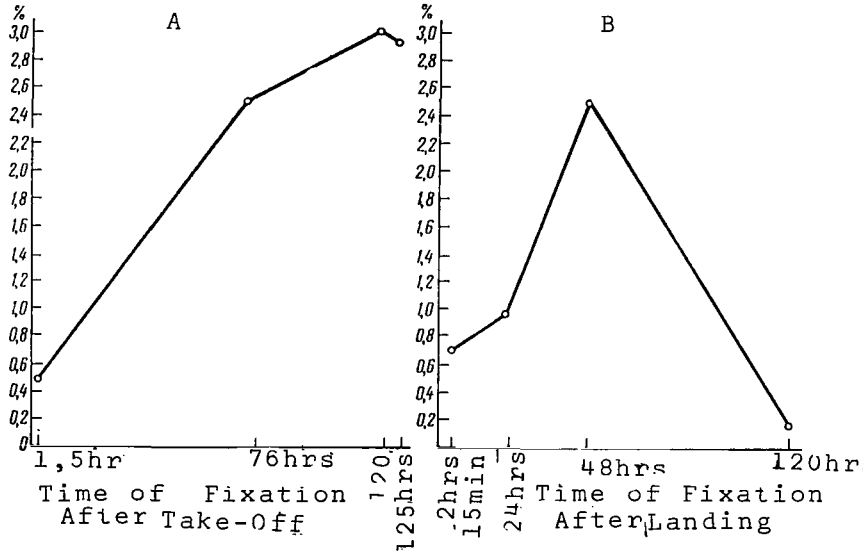

Fig. 4. Quantity of Cells with Mitotic Disorders (in %) Occurring During Flight Aboard the "Vostok-5" (A) and "Voskhod" (B).

TABLE 4. NUMBER OF CELLS WITH MITOTIC DISORDERS IN THE MICROSPORES OF TRADESCANTIA PALUDOSA, OCCURRING UNDER THE EFFECT OF FACTORS OF SPACE FLIGHT ABOARD THE "VOSTOK-5" AND "VOSTOK-6" SPACECRAFT. (ANALYSIS OF BINUCLEAR POLLEN)

Time of fixation of the materials	Phases of mitosis affected by the factors	No. of cells	Types of disorders			
			V		III	
			abs	%	abs	%
"Vostok-5" 1.5 hrs after launching.	Binuclear pollen	1000	—	—	19	1,9
"Vostok-5" ac 76 hrs after launching	Late Prophase, Metaphase, Anaphase, Telophase, Binuclear pollen	1000	1	0,1	21	2,1
"Vostok-5" 120 hrs after launching.	Middle, Late Interphase, Prophase Metaphase, Anaphase, Telophase, Binuclear pollen	1000	1	0,1	20	2,0
"Vostok-5" 3.5 hrs after landing.	the same	1000	1	0,1	29	2,9
"Vostok-6" 4.5 hrs after landing.	Late Interphase, Early, Middle, Late Prophase	1000	2	0,2	25	2,5
Control at the Cosmodrome	—	1000	—	—	1	0,1
Control at Moscow	—	1000	—	—	2	0,2

TABLE 5. NUMBER OF CELLS WITH MITOTIC DISORDERS IN THE MICROSPORES OF TRADESCANTIA PALUDOSA, OCCURRING UNDER THE EFFECT OF FACTORS OF SPACE FLIGHT ABOARD THE "VOSKHOD-1" SPACECRAFT. (ANALYSIS OF ANAPHASES AND TELOPHASES)

Time of fixation of the materials	Phases of mitosis affected by the factors	No. of cells	No. of disorders		Types of disorders									
					I		II		III		IV		V	
			abs	% ± m	abs	%	abs	%	abs	%	abs	%	abs	%
22 hrs.30 min afterlaunching	Middle, Late Prophase	105	1	0,95 ± 0,95	—	—	—	—	1	0,95	—	—	—	—
2 hrs 15 min. afterlaunching	Middle, Late Prophase	1651	12	0,72 ± 0,21	1	0,06	3	0,18	8	0,48	—	—	—	—
24 hrs after landing	EarlyProphase	1232	12	0,97 ± 0,28	2	0,16	4	0,32	6	0,49	—	—	—	—
48 hrs after landing	LateInterphase	2101	54	2,57 ± 0,35	15	0,71	26	1,24	9	0,43	3	0,14	1	0,05
120 hrs after landing	Early Interphase	3323	3	0,09 ± 0,05	2	0,06	—	—	—	—	1	0,03	—	—
Control at the Cosmodrome		1000	—	—	—	—	—	—	—	—	—	—	—	—

ploids and hyperploids. The phenomenon of primary non-separation of the chromosomes during the effect of space-flight factors on Drosophila was observed by N.P. Dubinin [4].

The fixation of the materials at various times after launching proved that the long duration of the flight aboard the "Vostok-5" led to an increase in the number of disorders in the mechanism of mitosis (see Figure 3). However, these same data could also be explained by the varying sensitivity of the mitotic orbits, if we assume that the peak of sensitivity occurs at the early interphase, and the sensitivity decreases as the mitotic orbits pass. We should note that the first fixation (1.5 hours after launching) made it possible to study the metaphasic cells, beginning only with the late prophase, while the last fixation (after 120 hours) showed cells which came into being during the flight, beginning with the early interphase (see Table 3). /337

The experiments aboard the "Voskhod-1" showed that the most sensitive orbit (the criterion for sensitivity was the number of cells with mitotic disorders) was the late interphase. Inasmuch as the entire flight lasted one full day, we determined the effect of all the factors of the space flight in the early interpahse by fixation 120 hours after landing; in the late interphase, by fixation 48 hours after landing; in the early prophase, by fixation 24 hours after landing; in the middle and late prophase, by fixation 2 hours and 15 minutes after landing.

Thus, we needed to conduct two experiments in order to show that the number of cells with mitotic disorders increases with an increase in the duration of the flight. Moreover, we know from the data from physical and biological dosimetry, that the background of radiation inside the craft during the flights was extremely low.

On the other hand, the accelerations and vibrations corresponding to the climb and descent must have been identical in all the cases for the experiments we mentioned. Therefore, of all the factors of a space flight, only the factor of dynamic weightlessness affected the cells to a greater degree as the duration of the flights increased. Thus, we must attribute any disorder in the mechanism for mitoses in the microspores to the effect of weightlessness.

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RADIATIONAL FACTOR

CHANGES OF CERTAIN BIOCHEMICAL INDICES IN ANIMALS DURING THE EFFECT OF ACCELERATION AFTER γ-IRRADIATION

Ye.A. Abaturova, V.V. Antipov, B.I. Davydov, and N. G. Demochkina

ABSTRACT: Tissue respiration and hydrogenase activity in the cerebrum, myocardium and small intestine were examined during the effect of acceleration on irradiated animals. There was a small increase in the tissue respiration and the activity of the glycerophosphatin dehydrogenase was decreased for two days. The changes in the tissue respiration in the cerebrum and myocardium were insignificant. There was an increase in the activity of the alkaline phosphatase in the tissue of the stomach.

The combined effect of dynamic factors and radiation was examined in a number of studies [1,4,6,15]; it was shown that accelerations and vibrations change the course of a radiation reaction. In addition, a number of experiments have been conducted to study the mechanisms for the distorted reaction of an organism to the combined effect of dynamic factors for flight and radiation. It has been shown that during the effect of acceleration and ionizing radiation, there are changes in the content of biologically active compounds (ceruloplasmin, serotonin, adrenalin, and noradrenalin [8,12]). /338

We had previously concluded that the changes in the serotonin content after acceleration and exposure to ionizing radiation are possibly caused by changes occurring in the gastrointestinal tract. Therefore, it seemed of definite interest to study tissue respiration, anaerobic glycolysis, and certain enzyme systems in the tissues of the stomach and the intestine, as well as in the cerebrum, myocardium, and skeletal muscle, in view of the significance of the latter in the general reaction of an organism to factors of space flight.

METHODS

The experiments were conducted on 50 white mice of no particular strain and 40 male mice of the SVA strain, weighing 19-22 g. The white mice were rotated in a centrifuge for 1 hour (10 g), while the mice of the SVA strain were rotated for 5 min (40 g). Some of the animals were rotated 10 days after a single general γ-irradiation with Co^{60} in a dose of 700 r (18 r/min). The mice were decapitated 30, min, 3-6 hours, and 1, 2, 5, 7, 8, 21, and 22 days after the effect of the accelerations.

In the cerebrum, myocardium, skeletal muscle (hip), and small intestine, we measured the tissue respiration (absorption of O_2 and respirational coefficient) according to the method of N.P. Mechkova and S.Ye Severin [7] and the anaerobic glycolysis (except for the small intestine), using the modification of the same authors. In carrying out the latter examination, incubation in a Warburg apparatus was replaced by storage for 2 hours in a thermostatic chamber at 37°. We determined the amount of lactic acid formed during this time with the aid of paraoxydiphenyl [7]. In the cerebrum, myocardium, skeletal muscle, and small intestine, we also determined the activity of the α-glycerophosphatic and succinic dehydrogenases by means of the change (by tissular extracts) of colorless triphenyl-tetrazole into red formazan [5]. The determination of the activity of the glycerophosphatic dehydrogenase allowed us to study the effect of accelerations on glycolysis and the presence or absence of a shift in the glycolytic process of an exchange of carbohydrates for lipids. /339

Moreover, in the extract from the stomach, we examined pepsin by the Hunt method in the modification of B.I. Sabsay [10]; in the extract from the upper third of the small intestine, we examined the alkaline phosphatase by the method of G.K. Shlygin.

RESULTS AND DISCUSSION

In evaluating the results obtained concerning the tissue respirations and the activity of the dehydrogenases, we must consider the fact that during the incubation of the tissular electuaries, we are artificially producing favorable conditions for the enzyme processes being studied (pH of the medium, oxygen supply, etc.). Therefore, if the enzymes did not undergo an irreversible inhibition, but their activity was merely suppressed as a result of a disorder in the oxygen transport, by placing the tissular electuaries under artificial conditions of incubation we can increase the activity of their enzyme systems in the same way, on the condition that the necessary substrates are present. The quantity of the latter can even exceed the norm if the blood circulation (and thus, the oxygen transport to the tissues) is disturbed. In such cases, in the experiments in vitro, we can find an increase in the oxygen requirement for the tissular electuaries, although it may possibly be decreased in the organism.

The absorption of oxygen by the small intestine was suppressed in both groups of mice (with and without irradiation, Table 1). However, this occurred only to a small degree, and only during the first hours after the accelerations. The respirational coefficient was halved for the first two days; in this case, there was a simultaneous occurrence of complete suppression of the activity of the succinic dehydrogenase. The tissue respiration (determined by the activity of the succinic dehydrogenase) was restored one week after rotation in the centrifuge. Three weeks later, there was a significant decrease in the activity of both dehydro-

genase. The data presented show a lack of normalization in the small intestine for the carbohydrate exchange, for a period of 3 weeks after the acceleration, particularly with irradiation (second group of mice). Of particular note is the general dehydrogenase activity which greatly exceeded the norm (without addition of substrates for the effect of the dehydrogenases) during the first hours after rotation with irradiation. This is caused, in our opinion, by an accumulation of glycolytic products in the small intestine as a result of disorders in the blood circulation. /340

In contrast to the respirational enzymes and glycolysis, the activity of the alkaline phosphatase sharply increased after the acceleration, particularly during irradiation, and it even greatly exceeded the norm for 3 weeks.

TABLE 1. TISSUE RESPIRATION (O_2 ABSORPTION, ml/2 HOURS IN 100 mg OF A TISSULAR ELECTUARY) AND ACTIVITY OF THE SUCCINIC AND GLYCEROPHOSPHATIC DEHYDROGENASES, ALKALINE PHOSPHATASE, AND PEPSIN IN THE SMALL INTESTINE AND THE STOMACH, FOR MICE OF THE SVA STRAIN, AFTER THE EFFECT OF ONE ACCELERATION AND 10 DAYS AFTER γ-IRRADIATION

Organ	Indices	Biological Control	Time after the Effect of an Acceleration: Acceleration (First Group) 3 hrs	1 day	7 days	21 days	γ-Irradiation+Acceleration (Second Group) 6 hrs	2 days	8 days	22 days
	Tissue Respiration									
	O_2	29,5	20,2	30,0	—	27,4	36,8	45,2	—	45,5
	CO_2/O_2	1,0	0,5	0,5	—	1,0	0,5	0,5	—	1,18
	Activity of the Dehydrogenase									
Small Intestine	Total Dehydrogenase Activity (Control), arbitrary unit	2720	3560	2090	1140	1780	7830	0	0	7360
	Succinic Dehydregenase, arbitrary units	4190	220	0	3620	2970	975	0	4770	5990
	Glycerophosphatic Dehydrogenase, arbitrary units	4190	3820	2950	3620	2390	8570	310	650	3140
	Digestive Enzymes									
Stomach	Alkaline Phosphatase, Arbitrary units	1330	—	2018	2328	1733	1200	4067	3273	2229
	Pepsin, arbitrary units	145	22,14	95,5	153,3	138,3	173	88,9	212,3	123

TABLE 2. TISSUE RESPIRATION (ABSORPTION OF O_2, ml/2 HOURS IN 100 mg OF A TISSULAR ELECTUARY) OF THE CEREBRUM, HEART, AND HIP MUSCLES, FOR MICE OF THE SVA STRAIN. /341

Nature of the Effect	Time After Effect	Cerebrum		Heart		Hip Muscles	
		O_2	CO_2/O_2	O_2	CO_2/O_2	O_2	CO_2/O_2
Biological Control		82,0	0,85	29,2	>1,0	9,3	—
Acceleration (First Group)	3 hrs	76,1	0,94	29,1	1,86	4,4	2,0
	1 day	77,6	0,77	22,2	0,70	20,2	0,75
	7 days	50,0	1,28	20,4	—	11,8	—
	21 days	73,5	1,0	15,0	0,5	14,4	1,64
γ-Irradiation+ Acceleration (Second Group)	6 hrs	59,2	0,6	17,0	1,30	14,8	0,7
	2 days	74,8	0,8	—	—	—	—
	8 days	—	—	—	—	—	—
	22 days	82,8	1,0	23,5	1,57	23,6	—

The pepsin content (Table 1) in the walls of the stomach changed in the same way for both groups of mice. The first increase in the activity of the pepsin, 3 hours after the acceleration, was noted in the mice of the first group. This increase was found to be the most significant. After two days, the activity of the pepsin in moth groups of mice was 30% lower than the norm, but it increased significantly around the eightth day, particularly after acceleration with irradiation. Three weeks after the effect, the pepsin content in the walls of the stomach for the mice of the first group practically reached the norm; for the mice in the second group, it was somewhat less.

The absorption of oxygen by the tissue of the cerebrum was close to the norm for the first two days after the acceleration, for the white mice and the mice of the SVA strain (Tables 2 and 3). A significant disorder of the tissue respiration in the cerebrum was observed for the SVA mice of the second group (with irradiation) after 6 hours; the oxygen absorption and respirational coefficient were simultaneously decreased, with a complete suppression of the succinic dehydrogenase. Three weeks after the acceleration, the absorption of oxygen by the brain (and the respirational coefficient) were within the limits of the norm, but the activity of the succinic dehydrogenase reached only 50% (Table 4). The anaerobic glycolysis in the cerebrum (experiments on white mice, Table 3) was greatly intensified immediately after the effect, and then decreased sharply to a point lower than the norm (Table 3).

TABLE 3. RESPIRATION AND ANAEROBIC GLYCOLYSIS IN THE CEREBRUM, HEART, AND HIP MUSCLES FOR WHITE MICE*, AFTER THE EFFECT OF ACCELERATION

Time After Acceleration	Cerebrum			Heart			Hip Muscles		
	O_2**, ml	CO_2/O_2	Lactic Acid**, γ	O_2, ml	CO_2/O_2	Lactic Acid, γ	O_2, ml	CO_2/O_2	Lactic Acid, γ
Biological Control	55,8	1,00	186	25,8	1,10	24	12,6	1,07	342
30min	59,4	0,88	288	13,5	2,20	118	15,6	3,0	200
24hrs	57,7	0,70	127	17,0	1,60	142	16,0	1,3	60
48hrs	61,0	1,35	160	26,6	3,0	—	6,0	2,0	—
5 days	30,8	1,35	32	13,7	2,0	144	7,0	3,0	256

* Average data for 10 animals
** Absorption of O_2 and formation of lactic acid in 100 mg of a tissular electuary, for 2 hours of incubation.

TABLE 4. ACTIVITY (IN ARBITRARY UNITS) OF THE SUCCINIC AND α-GLYCEROPHASPHATIC DEHYDROGENASES OF THE CEREBRUM AND HIP MUSCLES FOR THE MICE OF THE SVA STRAIN /342

Nature of the Effect	Time After the Effect	Cerebrum			Hip Muscles		
		Control*	Succinic Dehydrogenase	α-Glycerophosphatic Dehydrogenase	Control	Succinic Dehydrogenase	α-Glycerophosphatic Dehydrogenase
Biological Control		2900	19 940	4510	0	4250	340
Acceleration (First Group)	3hrs	—	—	—	0	0	320
	1day	0	0	240	0	0	470
	7days	0	1 775	180	0	200	240
	21days	0	11 530	1250	0	4950	1360
γ-Irradiation+ Acceleration (Second Group)	6hrs	920	0	2110	0	150	1030
	2days	—	—	—	0	0	120
	8days	720	5 860	1930	0	1730	260
	22days	0	10 820	670	0	5200	890

* without adding a substrate of succinate or α-glycerophosphate.

At the same time, the activity of the glycerophosphatic dehydrogenase also decreased almost to zero in the brain of the SVA mice in the first group (Table 4); it then amounted only 25% of the control value for the following 3 weeks. For the mice of the second group (with irradiation), the activity of the glycerophosphatic dehydrogenase in the cerebrum gradually decreased, and amounted to 10% of the activity for the enzyme in the controls for the following 3 weeks. The decrease in the absorption of oxygen by the myocardium in the SVA mice of the first group began one day after the acceleration, /343 and gradually reached one half of the norm during the following three weeks. However, the high respirational coefficient during the first hours after rotation shows that the tissue respiration during this time was disturbed. With irradiation, the oxygen absorption decreased almost by half within 6 hours after the acceleration.

In an experiment on white mice which were subjected to more prolonged effects of acceleration (Table 3), the oxygen absorption of the myocardium was decreased almost by half immediately after the effect; within two days it reached the norm, but again decreased by 50% around the fifth day. The respirational coefficient during these observation periods exceeded the control by a factor of more than 2.

The oxygen absorption for the hip muscles of the SVA mice in the first group was sharply suppressed 3 hours after acceleration (Table 2), then exceeded the norm by a factor of almost 2 on the first day following, and was somewhat higher than the norm by the end of the experiment. Except for the first days after the acceleration, when the respirational coefficient decreased by 25% against the background, it greatly exceeded the background during the remaining observation periods. Inasmuch as the succinic dehydrogenase (Table 4) was completely suppressed during the first week after the acceleration, we can assume that the normalization of the tissue respiration for the hip muscles began later (within 3 weeks after the rotation in the centrifuge). During this time, the activity of the succinic dehydrogenase was completely restored, but the simultaneously recorded respirational coefficient (1.67) shows the still incomplete normalization of the tissue respiration during this period. After acceleration with irradiation (second group), the oxygen absorption of the hip muscles greatly exceeded the norm, particularly after 3 weeks; the activity of the succinic dehydrogenase was also completely restored at this time. The simultaneous intensification of the activity of the glycerophosphatic dehydrogenase by a factor of more than 2 allows us to assume that the tissue respiration of the hip muscles for this group of mice was also still not normalized. A more significant intensification of the activity for the glycerophosphatic dehydrogenase to the same level was also noted in the mice of the second group within 6 hours after the acceleration; within two days, the glycerophosphatic dehydrogenase was at its lowest level ($\sim$ 33% of the norm); around the eightth day, it increased by a factor of 2, but still did not reach the norm.

In the experiment on the white mice, the oxygen absorption for the hip muscles exceeded the control level by 30% during the first days after the acceleration, and decreased by a factor of almost 2 during the following 5 days. The respirational coefficient was even higher than in the experiment on the SVA mice. The glycolysis, as in the experiment with the SVA mice, was most strongly suppressed (with irradiation) within 2 days after the acceleration. It was still not restored 5 days following the effect.

The above-mentioned experimental data indicate that the disorders in the carbohydrate exchange observed in an organism which is subjected to acceleration are caused primarily by stagnation /344
phenomena which lead to an accumulation of incompletely-oxidized metabolites in the tissues, particularly in the intestine and in the hip muscles. Obviously, this also was the cause for the intensification of the oxygen absorption during the first hours and days after the rotation in the centrifuge. There was a definite regularity in the change of the respirational coefficient. One day after the acceleration, it was much lower than during the first hours and the periods following the effect. During this period, there was also a complete suppression of the activity of the succinic dehydrogenase. Beginning with the seventh day, the activity of the succinic dehydrogenase began to increase, and reached the norm in the intestine and the hip muscles after 3 weeks, while it reached only half of the norm in the cerebrum. Obviously, complete normalization of the tissue respiration did not occur at this time. Another indication of the incomplete recovery of the tissue respiration after 3 weeks is the fact that the glycolysis (activity of the glycerophosphatic dehydrogenase) in the hip muscles of the SVA mice simultaneously increased by several times against the norm. The sharp intensification of the glycolysis during the insufficiency in the tissue respiration must be examined as compensatory. This provides for drawing the conclusion that the regulatory functions of the central nervous system, which affects the cardiac activity and the skeletal muscle, were restored very rapidly, if they were disturbed at all.

Of particular note is the lack of significant change in the tissue respiration of the cerebrum during the first hours after acceleration, and the simultaneous sharp intensification of glycolysis in the brain. The data in the literature indicate that there is protective inhibition in the cerebrum during this period [3]. The latter is the period of active recovery of the energy resources for the brain, and this increases its resistance to oxygen deficiency [2], obviously as a result of the intensification of glycolsis. The fact that within 3 weeks after the acceleration, the tissue respiration in the cerebrum (determined by the activity of the succinic dehydrogenase) is not completely restored, while the activity of the glycerophosphatic dehydrogenase (glycolysis) is sharply suppressed (particularly with irradiation) allows us to assume that the carbohydrate exchanges during this period are disturbed, and the synthesis of the lipids is intensified as a result

of an accumulation of glycerin--a phenomenon which is also observed after the effect of ionizing radiation on an organism [9, 13,14]. The simultaneous suppression of the respiration and the glycolysis (activity of the α-glycerophosphatic dehydrogenase) was observed particularly during the first week after the rotation.

All this taken together indicates that there are significant, slowly abating, disorders in the carbohydrate metabolism of an organism and in the activity of certain enzymes of the gastrointestinal tract which are produced by the effect of acceleration. Obviously, these changes are caused (to a great degree) by a disorder in the regulatory function of the cerebrum: first as a result of the presence of protective inhibition, and secondly because of /345 suppression of oxidation processes. The highly significant increase in the activity of the alkaline phosphatase in the small intestine (and pepsin in the stomach) with irradiation is possibly caused by a "superposition" of one effect on the other, leading to an even more significant disturbance of the regulatory function of the cerebrum. The effect of the latter on the secretory function of the stomach is also indicated by the increase in the excretion of pepsin during the first hours after rotation, when the cerebral cortex is in a state of protective inhibition. The excretion of pepsin on the first day after acceleration was increased by a factor of almost 2, which was obviously caused by its preceding intensified secretion. Judging by the suppression of the tissue respiration in the cerebrum, we also noted a simultaneous disturbance in the secretion of pepsin and alkaline phosphatase.

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HEMATOLOGICAL AND PATHOMORPHOLOGICAL CHANGES IN ANIMALS UNDER THE CONDITIONS OF AN EXPERIMENT WHICH MODELS THE EFFECT OF IONIZING RADIATION AND FLIGHT FACTORS ON AN ORGANISM

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ABSTRACT: A repeated preliminary irradiation of guinea pigs up to total doses of 50 and 75 r, with a following effect fractionated by 3 r, leads to changes in the composition of the peripheral blood.

The adrenocorticotropic hormone (ACTH) causes disorders in the blood system which are expressed in an intensification of the changes (and distortion of the reaction) on the part of the leukocytes, neutrophils, lymphocytes, and eosinophils in their response to radiation.

Within 1.5 months after the termination of the radiation, for a total dose of 90 r, the following are observed: a decrease of the follicles in the spleen, a decrease in the quantity of cellular elements and iron-containing pigment in the pulp, a thickening of the walls of the central arteries for the follicles of the spleen, and hemorrhages in the mucus of the stomach and the tissue of the lung.

Degenerative-dystrophic changes are found in the intramural apparatus of the urinary bladder of the irradiated animals.

In applying ACTH, the changes are more weakly pronounced during the recovery period.

It is well known that the effect of flight conditions causes /346
significant changes in the condition of various systems in an organism. Thus, the ionizing radiation during a space flight exerts its effect on an organism under the conditions of an altered functional state.

The changes in the characteristics of the peripheral blood, which occur under the influence of a combination of flight factors, coincide with those which occur during stress reactions and are characterized by the development of neutrophilic leukcytosis, relative lymphopenia, eosinopenia, and a decrease in the number of thrombocytes. As a rule, these changes disappear within one day after the end of the flight.

The changes on the part of the characteristics of the blood reflect the adaptative and stress reactions of an organism, in the realization of which the neuro-endocrine system participates actively [3,4,6,8].

The changes in the numbers of eosinophils and leukocytes occurring under the influence of flight conditions can be largely reproduced by administering an adrenocorticotropic hormone (ACTH), which participates in stress reactions. In relation to this, the functional stress on the blood system was reproduced in our experiments by administering this hormone in a quantity of 0.2 ml approximately 3 hours before irradiation; in this way, the responsive reaction of the blood system to the effect of flight conditions, and to the change in its functional state, was modeled.

As for the effect of ionizing radiation, we selected the following variation of their repeated effect: 28 days after irradiation repeated twice or three times at intervals of 15 days (within the limits of an acceptable dose = 25 r), the animals are subjected to the repeated effects of radiation in doses of 3 r, at intervals of 14-35 days (see Table).

The experiments were conducted on 25 guinea pigs of both sexes. The animals were divided into the groups shown in the Table.

The hematological examination of the animals was conducted on the evening before the irradiation and the administration of the ACTH, as well as 3 hours and one day after the effect. The absolute quantity of eosinophils was determined by the method of Bachman, using Hinkelman solution. The remaining characteristics of the blood were examined according to the generally-accepted method. Within 1.5 months after the end of the irradiation, the animals were killed and subjected to pathomorphological and histological /347
studies. Small pieces of the spleen, lung, liver, wall of the stomach, and bone marrow from the hip and sternum were put in Maksimov's fluid, fixed in celloidin, and stained with hemotoxylin-eosin. The hips and the sternum were decalcinated in a 10% solution of nitric acid with 5% formalin. When necessary, we determined the iron in sections of the spleen and the lungs by the Pearly method. The urinary bladder was fixed in 10% neutral formalin (partly in alcohol) and treated by the Bielschowsky-Gros method, the Campos method, and original methods used in the Department of Histology of the Volgograd Medical Institute for finding changes in the intramural nervous system.

RESULTS OF HEMATOLOGICAL EXAMINATIONS

The reactions on the part of the amount of erythrocytes were almost of the same type for the animals in all the groups. This reaction was characterized by an oscillation of this characteristic throughout the period of radiation in doses of 25 r. After radiation in doses of 3 r, the amount of erythrocytes decreased. This

was particularly noticeable in the animals of the second group, where the quantity of erythrocytes (after each radiation in a dose of 3 r) decreased by 0.8-1.3 million in 1 mm^3 of blood, in comparison with the lower limit for the original values. The animals of

DISTRIBUTION OF THE ANIMALS ACCORDING TO GROUPS

Group Number	Nature of the Effect	Days for Irradiation in Doses of 3 r, and for Administering ACTH
1	Preliminary radiation in a dose of 75 r	1-35-50-72-88th days; ACTH was not administered
2	Preliminary radiation in a dose of 75 r	1-35-50-72-88th days; ACTH was administered on the days of irradiation
3	Preliminary radiation in a dose of 50 r	1-35-50-72-88th days; ACTH was not administered
4	Preliminary radiation in a dose of 50 r	1-35-50-72-88th days; ACTH was administered on the days of the irradiation
5	Control for the Effect of the ACTH	No irradiation; ACTH was administered at the same times as for the experimental groups

the fifth group, which received only the ACTH, reacted to its administration by a small decrease in the number of erythrocytes; as a rule, this change was within the limits of the original values.

Three hours and one day after all the radiations in doses of 25 r, the number of leukocytes in the animals of the first group increased significantly, particularly after the first two effects, but it decreased by 2.4 thousand (in comparison with the lower limit for the original values) before the third radiation at this dose. The first, third, and fourth radiations in doses of 3 r led to a decrease in the number of leukocytes 3 hours after the effect, while the fifth administration of ACTH after the termination of the irradiation was accompanied by a certain increase in the number of leukocytes, which was recorded on the first day after the effect. /348

For the animals of the third group, which were subjected to preliminary radiation up to a total dose of 50 r, the changes in the number of leukocytes were similar to those described for the first group, but somewhat less pronounced.

In the second group of animals, after the first irradiation in a dose of 25 r and the administration of the ACTH, the number of leukocytes (which increased somewhat around the third hour after the effect) decreased by 1.7 thousand per 1 mm^3 of blood, in comparison with the lower limit for the original level. It then becam3

normal; during the second irradiation in a dose of 25 r, it exceeded the upper boundary for the original values by 1.5 thousand. After the second administration of the ACTH and exposure to this dose, there followed a brief and slight rise in the number of leukocytes, but their quantity fell to 1.4 thousand less than the original within one day. The third combined effect of the ACTH and radiation was immediately accompanied by a further and prolonged decrease in the number of leukocytes. Before the first irradiation in a dose of 3 r (i.e., after 28 days), it was 3 thousand less than the lower limit for the original data. After the first exposure to a dose of 3 r and administration of the ACTH, the number of leukocytes in the animals of the third group increased up to the original level, where it was maintained until the third combined effect. This effect and those following it caused a pronounced leukogenic reaction, when the number of leukocytes reached a level of 4-5 thousand lower than the original. The ACTH which was administered without irradiation on the fourteenth day after the combined effect caused an increase in the number of leukocytes after 3 hours, but after one day it was again 5.2 thousand less than the lower limit for the original condition.

Therefore, in the animals of the second group, the functional stress in the form of an administration of ACTH led to a more pronounced and prolonged leukopenic reaction, in comparison with that observed for the guinea pigs of the first group, which were irradiated in the same manner, but whithout preliminary administration of ACTH. Moreover, administration of the ACTH against the background of irradiation in doses of 3 r was accompanied in most cases not by a rise in the number of leukocytes in the animals of the second group, but (on the contrary) by a decrease in their number. In many cases, the same regularity (although less pronounced) was also observed in the guinea pigs of the fourth group. The only difference was that the leukopenic reaction of the animals of the fourth group to the combined effect appeared somewhat later. /349

It is important to emphasize that the administration of ACTH without irradiation was never accompanied by a decrease in the number of leukocytes. On the contrary, for the animals in the fifth group, the quantity of leukocytes was mainly higher than the original, or at the level of its upper limit. This circumstance shows that, for the animals of the second and fourth groups, there was no summation of the leukopenic effect for irradiation and administration of the ACTH, but there was a functional insufficiency in the blood system, which was most pronounced in the case of a preliminary fractionated irradiation up to a total dose of 75 r (25 r· 3). This is also indicated by the distortion in the leukocytic reaction to the administration of the ACTH, with subsequent irradiation. Another substantial fact is that, under these conditions, the repeated irradiation in doses of 3 r, combined with administration of ACTH, was also non-equilibious, since (for the animals of the fourth group) a significant leukopenic reaction was found in that period of the repeated effect of radiation in doses of 3 r.

The administration of the ACTH to the animals of the second and fourth groups, in combination with irradiation in doses of 3 r, always led to a less significant increase in the number of neutrophils. This indicates that the responsive neutrophilic reaction of the blood system in the irradiated animals to the administration of the ACTH was more weakly pronounced in comparison with that observed for the animals of the fifth group, which obtained the ACTH without irradiation. In other words, functional insufficiency of the blood system was found in this case.

The absolute quantity of lymphocytes for the animals of the first group underwent significant oscillations. There was a characteristic decrease in the quantity of lumphocytes after 3 hours and one day, for each irradiation in doses of 3 r, in comparison with the level 3 hours before the irradiation. In the intervals between irradiations, the number of lymphocytes again increased; at the time of the last irradiation, it was (as a rule) higher than the upper limit for the original values.

For the guinea pigs of the third group at the time of the fifth irradiation in a dose of 3 r and afterward, the number of lymphocytes decreased by 1-2.5 thousand, in comparison with the lower limit for the original values, but it again reached the original level within 2 weeks after this irradiation.

The characteristic feature of the reaction of the absolute number of lymphocytes in the animals of the second group was the fact that after the third combined effect of the ACTH and the irradiation in doses of 25 r and all the following effects in doses of 3 r, there was a brief but pronounced lymphopenic reaction. This appeared very clearly after the fourth and fifth irradiations in doses of 3 r, in combination with the ACTH. Within 3 hours after the effect, there were 5-6 thousand less lymphocytes than at the lower limit of the original value. After the third administration of ACTH and irradiation in a dose of 3 r, there was a decrease in /350
the general level of the quantity of lymphocytes. The pymphopenia in the animals of this group was found to be particularly stable; at the end of the observations, the quantity of lymphocytes was 3.5-3.8 thousand less than in the original condition.

In the fourth group of the animals which were subjected to radiation up to a total dose of 50 r along with the ACTH, there was also a significant (but somewhat less pronounced) lymphopenic reaction. With a repeated effect in doses of 3 r, the general level of the number of lymphocytes in the animals of this group also gradually decreased. Within 2 weeks after the fifth irradiation in a dose of 3 r, the number of lymphocytes averaged 3.4 thousand less than the original level.

For the animals of the fourth group, which obtained only ACTH, the changes in the absolute quantity of lymphocytes (just as for the animals of the first group) almost completely reflected the

dynamics for oscillation of the total number of leukocytes.

The reaction to administration of ACTH was the same for the animals of all the groups, 2 weeks after the termination of repeated irradiations in doses of 3 r. This reaction was characterized by a significant decrease in the number of lymphocytes 3 hours after administering the preparation. Within one day, there was a complete recovery of the number of lymphocytes in the animals of all the groups, except the second. In this group, there was practically no increase in the number of lymphocytes observed one day after the administration of ACTH.

The absolute quantity of eosinophils also underwent definite changes. For the animals of the first and third groups, which were subjected only to the radiation effect, each irradiation until the 35th day of the experiment was accompanied by a brief decrease in the number of eosinophils, with subsequent normalization. Three hours after the second irradiation in a dose of 3 r (35th day of the experiment), the number of eosinphils for the animals of the third group also decreased by 50% (in comparison with the level before the irradiation) but no normalization appeared after one day. Until the end of the experiment, the number of eosinophils for the animals of the third group averaged about 50% of the original values.

For the animals of the first group (which were irradiated up to a summary dose of 75 r) after the third and subsequent irradiations in doses of 3 r, the general level of the number of eosinophils rose progressively; however, within 3 hours after each sequential effect, there was a regular decrease, with a following increase after one day. On the 89th day of the experiment, with fractionated irradiation in a dose of 3 r, the quantity of eosinophils in the animals of the first group averaged 775% of the original level, while it average 700% on the 102nd day.

For the guinea pigs of the second and fourth groups, which obtained preliminary total doses of 75 and 50 r against the background of the effect of the ACTH, there were also oscillations in the quantity of eosinophils, but (as a rule) they were more strongly pronounced than for the animals of the first and third group.

Therefore, the administration of ACTH to the irradiated animals/351 caused, as a rule, much greater oscillation of the number of eosinophils (in the form of an increase in their quantity) one day after the combined effect than was observed for the animals of the fifth group, to which ACTH was administered without irradiation. This particular feature was more apparent in the animals of the second group, which obtained preliminary irradiation up to a total dose of 75 r.

As for the quantity of thrombocytes, we could not find any clear and regular changes, since the oscillations of this characteristic were also significant in the original state. Nevertheless,

we can establish that, after the period of repeated irradiations in doses of 25 r, there was a gradual decrease in the general level of the number of thrombocytes. In particular, the number of thrombocytes averaged about 160 thousand per cc of blood (in comparison with the 350 thousand of the original condition) one day after the third irradiation in a dose of 25 r for the first and second groups, and after the third administration of the ACTH for the fifth group. The number of thrombocytes remained at this level for the animals of these groups for 28 days. At about this time, the amount of thrombocytes also decreased (on the average, down to 185 thousand) for the animals of the third and fourth groups, which had obtained 2 irradiations in doses of 25 r. Repeated irradiations in doses of 3 r, in combination with ACTH and without it, were accompanied by fairly significant oscillations in the number of thrombocytes within a range of about 60-70% of the average original level; these oscillations did not have any definite directionality. We did not find any differences by groups for these oscillations.

Having generalized the results of the hematological observations on the guinea pigs, we can say that the effect of irradiation, the combined effect of irradiation in small doses and ACTH, and ACTH alone, caused rather pronounced changes in the morphological composition of the blood of the animals. It is important to emphasize that with the aid of the ACTH, which we used as a functional stress, we could find functional changes in the blood system of the animals which were subjected to preliminary repeated irradiation up to total doses of 75 and 50 r, and to subsequent repeated irradiations in doses of 3 r. In this case, it was found that the application of the functional stress reveals a relationship between the reaction of the blood and the dosage, even at such low levels of irradiation. A confirmation of this statement can be found in the fact that, for the animals of the second group, which received preliminary irradiation up to a total dose of 75 r in combination with ACTH and subsequent repeated irradiation in doses of 3 r, all the changes in the composition of the blood were more clearly pronounced than in the animals of the fourth group, which received preliminary irradiation up to a total dose of 50 r. It is essential to realize that the changes in the blood occurred not only during the period of the repeated irradiations in doses of 25 r, but were preserved and even progressed throughout the period of repeated irradiation in doses of 3 r. This is related to the development of leukopenia, lymphopenia, neutropenia, and intensification of distortion in the leukocytic and eosinophilic reaction /352
to the administration of ACTH. We can consider that the repeated irradiation in doses of 3 r occurred against a significantly altered functional background which was created by the preliminary irradiation up to a total dose of 75 or 50 r. This disadvantageous background was produced despite the fact that the preliminary irradiation in a dose of 25 r was made at intervals of 15 days, while there was an interval of 28 days between the last irradiation at this dose rate and the first irradiation in a dose of 3 r. The intervals between irradiations in doses of 3 r were also fairly long.

Nevertheless, we can see that complete recovery of the disordered functions does not occur for the given regime of irradiation.

RESULTS OF PATHOMORPHOLOGICAL AND NEUROHISTOLOGICAL EXAMINATIONS

Six weeks after the end of the fractional irradiation, amounting to a total dose of 90 r, we observed destruction of the follicles of the spleen in the guinea pigs, and a decrease in their size. A reticular stroma was found in areas around the periphery of the follicles. The lumina of the central arteries were somewhat expanded, and their walls were thickened. We found phagocytic nuclear fragments in small quantities in the follicles. The pulp of the spleen was impoverished in cellular elements, and the quantity of iron-containing pigment was decreased. Foci of extramedullary hemopoiesis were found less frequently than in intact animals. In the bone marrow, there was sometimes an increase in the quantity of cellular elements, and an increase in the dimensions of the cells in the endosteum.

In the lungs, there were signs of non-uniform hyperemia and areas of emphysema and atelectases. In one animal, there were punctate subpleural hemorrhages. In the same animal, there was a small defect of the epithelium of the gastric mucosa, with a hemorrhage and an inert inflammatory reaction.

For the irradiation in a total dose of 65 r, the pathomorphological changes were limited to a small decrease in the volume of the follicles of the spleen and a smaller quantity of iron-containing pigment in the pulp. In one aminal, there was erosion of the gastric mucosa, while there were very small foci of dispersing hemorrhages in the lungs, shown by the presence (in the alveoli) of cells of desquamated epithelium containing hemosiderin. In the remianing animals, the changes were the same as in the preceding group.

In the animals to which ACTH was administered before each irradiation (total dose of 90 r), the described changes were less pronounced. We could determine the reaction of the spleen to the radiation only by a certain blurring of the boundaries of the follicles. In the pulp of the spleen, the iron-containing pigment was found in greater quantity than for irradiation without preliminary administration of ACTH, but there was still less of it than in the control animals. In one animal, two foci of erosion were found /353 in the gastric nucosa, each having a diameter of about 0.5 cm, with an inert inflammatory reaction.

For the irradiation in a total dose of 65 r in combination with administration of ACTH, there was a decrease in the quantity of iron-containing pigment in the spleen, in comparison with the normal.

In one non-irradiated animal which had received ACTH, there

were several eroded segments located in gastric mucosa, and there was a large focus of disseminating pneumonia in the lungs.

Among the intact animals, no pathomorphological changes were found in the organism.

During the neurohistological examinations of the urinary bladder, we found the following. In the intact animals, there were often binuclear neurons with multiple processes in the ganglia, which had good vascularization. Among the clustered receptors located in the wall of the urinary bladder, there was a large quantity of polyvalents. The pericellular and pericapsular apparatus arose because of the delicate terminals of the nerve fibers. Even the synapses had small dimensions and the shape of rings or buttons; they were closely adjoined to the perikaryons of neurons, or were imbedded in the neuroplasm. In the urinary bladder of the animals which had received only ACTH, some of the ganglionic cells were somewhat enlarged; the satellites around them had multiplied rapidly. The terminals of some receptors had a delicate varicosity around their paths, and had become hyperchromic. The nerve fibers of the pulp were primarily involved in the reactive processes.

The fractional repeated irradiation of the animals with total doses of 90 and 65 r led to unique changes of a degenerative nature in the nerve apparatus of the urinary bladder, regardless of the value of the dose. The nerve nodes contained a large number of cell shadows. Their corpora became swollen, the satellite reaction increased sharply, and there was occasional pseudoneuronophagia. The number of binuclear and binucleolar ganglionic cells increased. The nerve fibers became varicose, with unequal notched borders and vacuoles. Some of the fibers of the internuscular and adventitious plexi underwent disintegration. At the sites of branching of the afferent fibers, infiltrations of the neuroplasm were seen. The terminals of the recptors became varicose and swollen, the terminal regions became enlarged, and, in contrast to many neurons, they were very hyperchromic. The receptors linked to the blood vessels underwent the greatest changes. The synapses became coarse and swollen, and were moderately enlarged.

In the animals which had received ACTH before irradiation, there were morphological changes which were typical of the reactive processes. Some of the nerve cells were in a state of amitosis; dumb-bell-shaped nuclei and incipient plasmotomy were very noticeable. Internodulary intraneuronic links were very clear, and were /354
characterized by an increase in the synaptic patches. The reactive changes greatly encompassed the intermuscular plexus, which was functionally the most active part. The afferent and efferent endings were fairly hypertrophic. Most of the pericellular apparatus had a regular form: in some nerve fibers, there were regional proliferations in the form of glomi. The Schwann cells, located at the sites of the dichotomic branching of the afferent fibers, were swollen and enlarged.

The changes found in the hemopioetic organs agree with the data in the literature. In response to the effect of ionizing radiation, the earliest morphological reactions are observed in the hemopoietic organs, in the form of a decrease in the volume of the follicles of the spleen, a degeneration of the lymphocytes in them, and an impoverishment of cellular elements in the bone marrow [7,10].

The vascular changes are also generally known to be part of the reaction to ionizing irradiation [1,2,7,9]. Their principal role is found in the appearance of a hemorrhagic syndrome during radiation sickness. The primary reaction of the vessels, according to the indications of the authors, is the plasmatic impregnation and the increase in the permeability of the vascular walls. After this, the walls of the vessels lose their shape and become homogeneous.

Obviously, the focal hemorrhages in the gastric mucosa and the development of erosions, certain changes of the walls in the central arteries of the follicles of the spleen, and the non-uniform hyperemia of the lungs can be indirect signs of incipient injury to the vessels.

According to the data of G. Heineke and A.Ye. Pareyshvili [10], the quantity of iron-containing pigment in the spleen during the first days after irradiation increases somewhat. E.I. Shchebran' [11] found a direct relationship between the radiation dose and the percentage of iron in the spleen of animals at the height of radiation sickness. However, around the 44th day and the period following (the observations were conducted up to 114 days), the author did not find any iron in the spleen. It is well known that after irradiation there is a massive destruction of the erythrocytes [5], and the quantity of iron-containing pigment in the spleen increases. However, the utilization of the iron is disordered, which subsequently leads to its disappearance from the spleen. In our experiment, the moderate decrease in the quantity of iron-containing pigment in the spleen of the guinea pigs after irradiation should obviously be considered as a sign of a disorder in the iron exchange which is found even during the remote after effects of repeated irradiations.

In the animals which were given ACTH, the impoverishment of lymphocytes in the follicles of the spleen, the disorder in the iron exchange, and the changes in the blood vessels were less pronounced than in the guinea pigs which were merely irradiated.

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COMPLEX EFFECT OF CERTAIN TYPES OF IONIZING RADIATION AND DYNAMIC FLIGHT FACTORS ON THE HEMOPOIETIC ORGANS OF MICE (PATHOMORPHOLOGICAL STUDIES)

N.A. Gaydamakin, V.G. Petrukhin, V.V. Antipov, P.P. Saksonov, and V.S. Shashkov

ABSTRACT: It was shown that the preliminary effect of a single vibration, 3 days (and particularly 1 day) before irradiation with protons (830-875 rad), intensified the damage to the lymphoid tissue in the spleen and lessened the damage to the hemopoietic cellular elements of the myeloblastic and erythroblastic growths in the spleen and bone marrow. The recovery of all types of hemopoietic tissue in these organs was accelerated. The effect of vibration (3 days and, particularly, 5 days after the irradiation with the protons) intensified the destructive changes in the hemopoietic organs. During the recovery period, foci of necrosis were found in the spleen and bone marrow, and the reparative processes were delayed. The effect of acceleration, applied one day before the γ-irradiation, decreased the devastation of the hemopoietic organs and accelerated their recovery. The effect of acceleration, applied one day after the γ-irradiation, had no definite relation to the degree of the radiation damage to the hemopoietic organs.

It has been shown in a number of articles that the reactions /355
of an organism to radiation undergo substantial changes when the radiation is combined with dynamic factors [3-5, 8-10].

In this study, we examined the dynamics of the pathomorphological changes in the spleen and bone marrow of 287 male mice of the C57bl strain, divided into 11 series.

The combined effect of incident radiation and vibration was examined in animals which were irradiated by a collimated beam of protons with an energy of 660 MeV, in doses of 830-875 rad, at the rate of 400-600 rad/min in the 6-meter synchrocyclotron of the Joint Institute for Nuclear Research. Two series of animals were subjected to the effect of a single vibration at a frequency of 70 Hz and vibration stress of 10 g for one hour, before irradiation (1 or 3 days before), and two other series were subjected to this

effect after irradiation (3 or 5 days later).

In examining the effect of the accelerations, on the duration /356 of the radiation injury, we used γ-irradiation from Co^{60} in a dose of 700 r, at the rate of 18 r/min. The animals were subjected to the effect of stresses repeated 10 times (10 units, 30 min) one day before and one day after the irradiation. Moreover, the mice of one series were subjected only to irradiation by the protons, while the mice in other series were subjected only to γ-irradiation, vibration, or accelerations.

For the pathomorphological studies, we killed the mice with ether after various periods (from 1 to 60 days after the effect). The spleen and bone marrow were fixed in a Carnot mixture and fixed in celloidin. The spleen was stained with hematoxylin-eosin and (according to Brashe) with methyl green-pyronine with a control of ribonuclease, while the bone marrow was stained only with hematoxylin-eosin. For the cytological control, we used smears of the bone marrow and prints of the spleen which were stained according to Pappenheim and Brashe (methyl green-pyronine).

The clinical symptoms of radiation sickness were almost identical for the irradiated animals of all the series. Around the 45th day, we could see foci of epilation covered with dry scales and bits of gray hair from 3 to 7 mm in diameter on the skin (Fig. 1). In the non-irradiated mice, individual gray hairs were found on the 45th and 60th days.

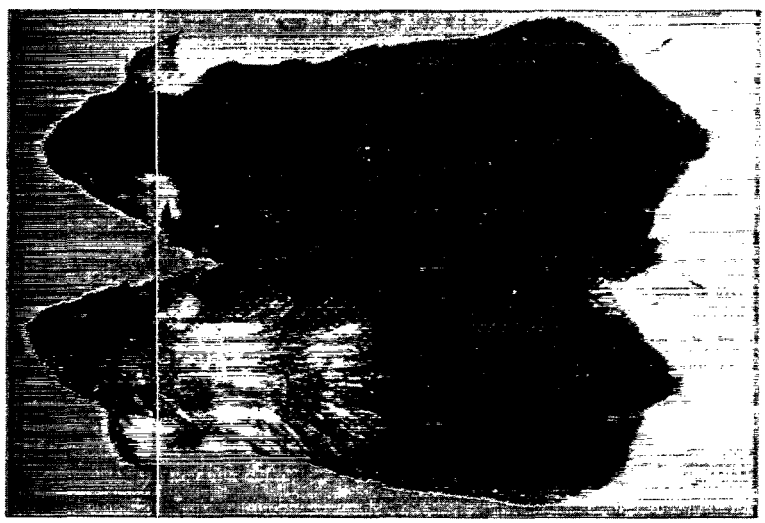

Fig. 1. Concentration of Gray Hairs on the Head and Back of a Mouse, 60 Days After Irradiation with Protons. In the Intact Animal, There are Individual Gray Hairs.

During the microscopic examination of the spleen, we found /357
that the follicles were decreased and poor in lymphocytes on the third day after irradiation. Around the central arteries and in places around the trabecules, we could see accumulations of reticular cells with pyroninophilic cytoplasm, among which we found cells with figures of mitosis. The myeloid foci disappeared from the pulp. The megakaryocytes that were preserved had hyperchromic pyknotic nuclei. On the seventh day, the dimensions of the follicles and the quantity of lymphocytes in them decreased even more. Around this time, lymphoblasts appeared in the follicles, and the number of cells with figures of mitosis increased. In the pulp, cells with a pyroninophilic cytoplasm were often found; among them, in addition to the hemocytoblasts, there appeared accumulations of erythroblasts, infrequent myeloblasts, and larger megakaryocytes. On the fifteenth day, the follicles had their regular dimensions, but there were few lymphocytes in them, and many lymphoblasts and prolymphocytes, often with figures of mitosis. In the pulp, we found a large amount of megakaryocytes and accumulations of erythro-, myelo-, and hemocytoblasts, among which we could see many mitotically dividing cells. On the thirtieth day, the quantity of lymphocytes in the follicles increased, and reproduction centers appeared in some follicles. The myeloid hemopoiesis was represented by polymorphocellular strands located in the pulp beneath the capsule and around the trabecules. In comparison with the preceding period, the quantity of erythro- and myelo- blasts and megakaryocytes among the myeloid cells increased, and the quantity of hemocytoblasts decreased. On the 60th /358
day, the follicles of the spleen had somewhat blurred boundaries, were of the usual dimensions, and contained a significant quantity of lymphocytes and somewhat more than the usual amount of prolymphocytes and lymphoblasts. Around this time, reproduction centers

Fig. 2. Myeloid Foci in the Pulp of the Spleen of a Mouse, 30 Days After the Effect of Vibration (Hematoxylin-Eosin, 210X.

were formed, the foci of the myeloid hemopoiesis decreased in volume, and the mitotic activity of the cells in them also decreased.

In the mice which were subjected to the effect of the vibration, we observed in the spleen (during the first days) a weakening of the mitotic activity of the hemopoietic elements in the follicles, as well as foci of myelopoiesis, an impoverishment in lymphocytes for the follicles, and destruction of some of the megakaryocytes. After the third day, we noted an accumulation of reticular cells in the follicles and the pulp; ribonucleic acid was found in the cytoplasm of these cells. By the seventh day, the number of hemocytoblasts had increased; around the 15th day, they were found much more often in the pulp of the spleen, beneath the capsule and around the trabecules, than was the case in the intact animals. The follicles of the spleen had almost completely recovered their volume by this time, and they contained the regular quantity of lymphoid elements. During the following period (on the 30th and 60th days), the quantity of myelopoietic foci in the pulp of the spleen increased, in comparison with the spleens of the intact mice (Fig. 2).

In the bone marrow of the animals which underwent the effect /359 of vibration, there was a development of venous plethora, erythrostases, and hemorrhages; there was also a definite expansion of the venous sinuses (Fig. 3). Around the third day, all these changes disappeared. During the following period, there was an increase in the quantity of nucleosegmental granulocytes in comparison with the bone marrow of the intact animals.

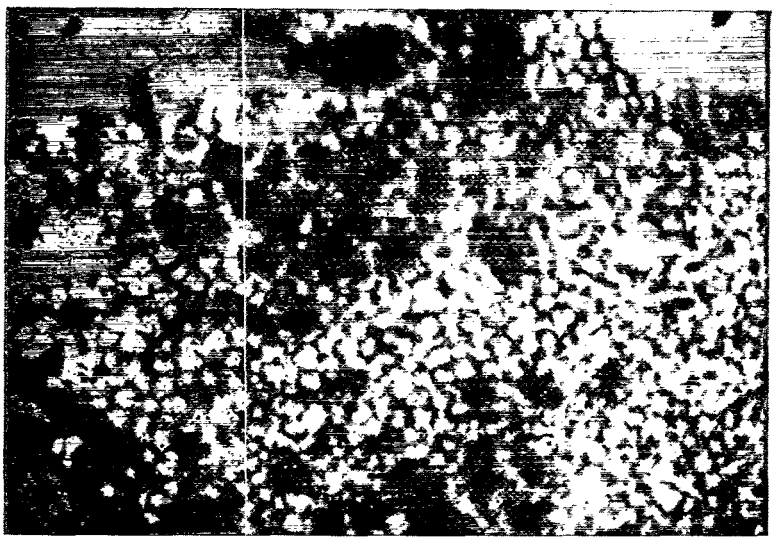

Fig. 3. Hemopoiesis in the Stroma of the Bone Marrow of a Mouse, 6 Hours After the Effect of Vibration (Hematoxylin-Eosin, 633X.)

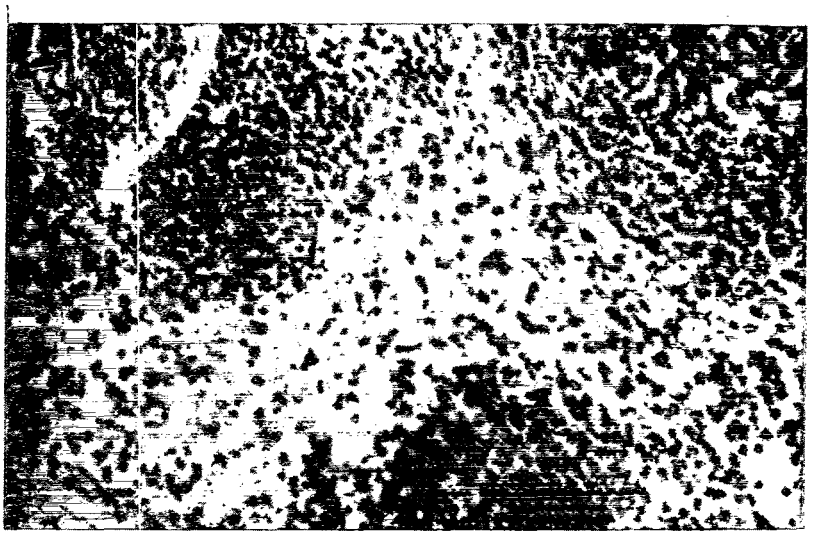

Fig. 4. Focus of Reticular Cells with a Basophilic Cytoplasm in the Pulp of the Spleen (Around the Trabecules), on the Third Day After Irradiation with Protons. One Day Before Irradiation, the Mouse was Subjected to the Effect of Vibration (Hematoxylin-Eosin, 320X.)

Fig. 5. Focus of Erythroblasts in the Bone Marrow of a Mouse, on the Third Day After the Combined Effect (Hematoxylin-Eosin, 320X.)

In the animals which were subjected to the effect of vibration one day before irradiation with protons, the nature of the pathomorphological changes was somewhat different from that observed in the mice which underwent only irradiation with protons. Thus, on the third day after irradiation, the follicles were decreased to the same degree, but they had fewer mature lymphocytes, and more reticular cells with a pyroninophilic cytoplasm and figures of mitosis than for the animals which underwent only the irradiation. In the pulp, we could see foci which consisted mainly of reticular cells with a pyroninophilic cytoplasm and a hyperchromic nucleus; some had figures of mitosis, as well as erythroblasts (Fig. 4). On the seventh day, the follicles of the spleen were larger, and they contained prolymphocytes with a higher mitotic activity, than after irradiation by protons. These follicles also contained lymphocytes. In the pulp of the spleen, we found erythroblasts more frequently and megakaryocytes less frequently. On the fifteenth day, there were many more lymphocytes, prolymphocytes, and mitotically dividing cells in the follicles of the spleen than were found in the animals after irradiation with protons. In the pulp, myeloid polymorpho- /360
cellular strands, consisting of accumulations of frequently-dividing (mitotically) erythroblasts, hemocytoblasts, and megakaryocytes, were found very often and in large quantities.

On the 30th day, the follicles of the spleen had normal dimensions, rather clear boundaries and formed multiplication centers, and contained more lymphocytes than were found in the animals after irradiation with protons. There were fewer cells with figures of mitosis. In the pulp of the spleen, there were more erythroblasts and myeloblasts and fewer hemocytoblasts. On the 60th day after the combined effect, the animals showed somewhat more lymphocytes in the follicles, and fewer myelopoietic foci in the pulp, than was the case for the mice which underwent only proton irradiation. However, the differences in this case, in comparison with the spleens of the animals which were only irradiated with protons, were less clearly expressed.

The bone marrow of the animals which underwent the effect of vibration one day before irradiation with protons was devastated (on the third day after the ionizing effect) to the same degree as the bone marrow of the animals which underwent only the proton irradiation. In the case of the combined effect, erythroblasts were found much more often in the bone marrow (Fig. 5). By the 7th day, the quantity of nucleosegmental granulocytes and megakaryocytes in the bone marrow of these animals had not changed. The quantity of erythroblasts increased to a lesser degree than for the animals /361
which underwent only the proton irradiation. Around the 15th day, the stroma of the bone marrow was almost completely filled with cellular elements; however, after the combined effect, there were many more developing hemocytoblastic forms in it. Around the 30th day, the quantity of mature cellular elements in the bone marrow had recovered almost to the original level, but they were found comparatively more frequently in the animals which underwent the

combined effect. By the 60th day, the bone marrow had the same structure as in the non-irradiated animals.

The damage to the bone marrow in the animals which underwent vibration 3 days before irradiation was less pronounced than for the animals which were only irradiated. However, it was more pronounced than for the animals which underwent vibration one day before proton irradiation. The recovery of the number of cellular elements, as in the two preceding series, began with an increase in the number of erythroblasts and hemocytoblastic elements, and occurred somewhat more slowly than in the animals which were irradiated with protons one day after the vibration. On the 30th and 60th days, there were no differences in the structure of the bone marrow for either series of animals which underwent the combined effect of protons and vibration.

After the combined effect of irradiation and subsequent vibration, the picture of the radiation injury also changed. For the animals which underwent vibration on the third day after proton irradiation, the destruction of the lymphoid elements in the spleen was intensified, all the way to their complete disappearance from the reticular stroma of the follicles. The recovery of the lymphoid tissue in the spleen was also delayed, while the recovery of the myeloid hemopoiesis occurred somewhat more rapidly. The damage to the bone marrow was also intensified, and the reticular stroma seemed to be more damaged on the third and seventh days. The erythroblasts disappeared entirely on the third day after irradiation (6 hours after vibration), and nucleosegmental granulocytes made up the main mass of the cells. During the following period, there was a definite retardation of the recovery of the cellular elements, principally the erythroblasts.

On the fifth day after irradiation with protons, and 5 hours after vibration, the spleen was wrinkled, there were almost no cells with figures of mitosis in the damaged and diminished follicles, and the nuclei of the reticular cells were sharply hyperchromic. The erythroblasts which were found in small amounts in the pulp had pyknotic nuclei. Recovery of the volume and cellular composition of the follicles and myelopoietic foci of the pulp was delayed. In the bone marrow, in addition to the intensification of the destruction of the hemopoietic cells, there was observed for a long time a detachment of the endosteum caused by a serious-sanguinolent fluid. The recovery of the bone marrow began later than in the animals which were only irradiated, and the maturation of the cellular forms in them was delayed. Moreover, on the 15th day after /363
vibration (on the 20th day after irradiation), we could see very large foci of necrosis in the spleen and bone marrow (Fig. 6).

The combined effect of incident radiation and acceleration was studied in animals which had been subjected to γ-irradiation. In the control series of animals which underwent only the γ-irradiation, the small number of lymphocytes remaining after one day in

the already very damaged follicles had pyknotic nuclei; we frequently found nuclear fragments; there were no cells with figures of mitosis. In the pulp, the volume of the myeloid foci sharply decreased. On the third day, there were no lymphocytes in the follicles. No myelopoietic foci could be found in the pulp, and there were few megakaryocytes. By the seventh day, the megakaryocytes had also disappeared. On the 15th day, there appeared lymphoblasts and prolymphocytes (some with figures of mitosis) in the follicles. Mature lymphocytes were found only along the periphery of the follicles.

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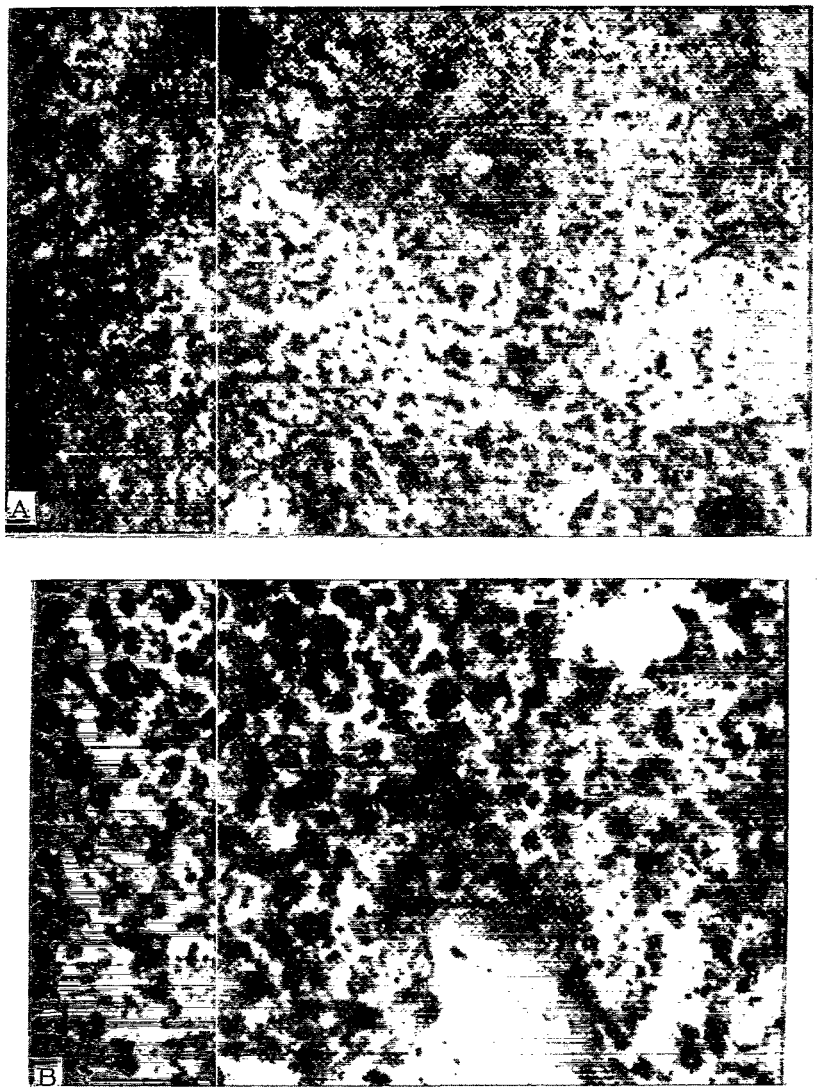

Fig. 6. Necrosis of a Follicle in the Spleen (A) and Bone Marrow (B) on the 20th Day After Proton Irradiation. On the 5th Day After Irradiation, the Mouse was Subjected to Vibration (Hematosylin-Eosin, 320X.)

The foci of myeloid hemopoiesis which appeared in the red pulp around this time consisted mainly of young hemocytoblastic elements with intensely pyroninophilic cytoplasm and high mitotic activity; more mature forms (erythroblasts and myeloblasts) were found rather infrequently. The percentage of megakaryocytes was the same as for the non-irradiated animals. On the 30th day, the quantity of mature cellular elements in the follicles and myelopoietic foci (in comparison with the previous period) increased, while the quantity of young non-differentiated cells decreased somewhat. The follicles were diminished, and they had no clear boundaries or reproduction centers. One day after the irradiation, there was a significant impoverishment in cellular elements in the bone marrow, and nuclear fragments were detected among the intact cells. On the third and seventh days, the bone marrow was devastated, and its stroma was surrounded by, and filled with, blood. Around the 15th day, there appeared focal accumulations of hemocytoblasts, erythroblasts, megakaryocytes and myeloblasts, but a significant part of the bone marrow still remained rather impoverished in cellular elements. On the 30th day, the bone marrow contained the regular quantity of cells; in this case, it differed from the bone marrow of the non-ir irradiated mice by a much higher percentage of young cellular elements.

For the mice which underwent the effect of acceleration (10 g for 30 min), we noted a rather diverse picture in the spleen and bone marrow during all the periods in some animals, the histological structure of these organs was usual; in others, there were certain changes. Thus, in some of the animals, the follicles of the spleen had blurred boundaries, and were somewhat impoverished in lymphoid elements; the mitotic activity of the latter was somewhat decreased. Between the cells of the follicles, there were /364
sometimes nuclear fragments; on the following days, they could not be found. An increase in the mitotic activity of the cells in the follicles of the spleen was noted up to the third day, while a lack of clarity in the boundaries of the follicles was maintained up to the seventh day. During the following periods, the morphological picture of the spleen for the mice which underwent the effect of acceleration was the usual one. After one day, some mice showed a definite increase in the quantity of erythroblasts and myeloblasts, and a decrease in the number of nucleosegmental granulocytes. Figures of mitosis were found among the megakaryocytes. During the following periods, the structure of the bone marrow was regular in most of the mice which underwent the stress; in some of them, the number of erythroblasts increased.

For the animals which underwent γ-irradiation one day after the acceleration, the changes in the spleen around the third day were the same as for the animals which were only γ-irradiated, but a small amount of lymphocytes remained in the follicles, as well as single figures of mitosis among the reticular cells. The latter could also be observed on the seventh day; at this time, single megakaryocytes were still preserved in the pulp. Around the 15th

day, in the animals which were subjected to the combined effect, the volume of the follicles was somewhat larger and there were more lymphocytes. Around the 30th day, after the γ-irradiation and after the combined effect, there was no significant difference found in the morphological picture of the spleen for the animals. Only on the seventh day were there certain differences in the bone marrow; they consisted in the fact that in those animals subjected to the combined effect of acceleration and γ-rays, the accumulations of erythroblasts in the stroma had a greater volume than in the animals which received only γ-irradiation. During the remaining periods, the picture was identical for both types of animals.

In the animals which underwent acceleration one day after γ-irradiation, the symptoms of radiation sickness and the pathomorphological changes in the hemopoietic organs of the mice during the proton irradiation in a dose of 830 rad (as well as during γ-irradiation in a dose of 700 r) had the same nature, although the degree of damage varied somewhat. For the proton irradiation, the destructive changes in the hemopoietic organs were less pronounced, recovery occurred more rapidly, and the spleen and bone marrow had almost normal structures around the 30th day. After the γ-irradiation, there was no recovery of the hemopoietic organs by the 30th day. Such differences, despite the levels of the doses for the protons and γ-rays being very close in value, could be explained by the fact that the relative biological effectivity of the protons, in relation to the γ-rays, is less than a unit [1, 11, 12, 15].

The effect of a single general vibration of 70 Hz for one hour /365 caused an impoverishment of lymphoid elements in the follicles of the spleen and destruction of a small number of hemopoietic cells. The regular structure of the spleen was restored around the 15th day. On the 30th and 60th days after the vibration, there was an intensification of myelopoiesis in the spleen. In the bone marrow, venous stasis appeared during the first hours after the effect; hemorrhages also appeared, which then disappeared by the third day. During all the following periods, there was an increase in the number of nucleosegmental granulocytes in the stroma of the bone marrow, which was obviously the result of an accelerated maturation of the cells in the myeloblast group. The results obtained confirm the data in the literature concerning a certain suppression of the lymphopoiesis in the spleen which occurs by the effect of vibrations; they also agree with the studies in which leukocytosis was found with relative lymphopenia in humans and animals during the effect of vibration [2, 13, 14].

In isolating the effect of acceleratoins of 10 g, we observed certain transient destructive changes in the spleen and bone marrow. These changes were less pronounced than in the case of the vibration.

The combined effect of ionizing radiation (of protons or γ-rays) and the single vibration or accelerations somewhat changed the

course of the morphological changes in the spleen and bone marrow.

Thus, for the effect of a vibration 3 days and, in particular, one day before the irradiation of the protons, the devastation of the follicles and their impoverishment of lymphocytes were intensified, and the destruction of myelopoietic foci in the pulp was decreased. The restoration of the follicles and the foci of myeloid hemopoiesis in the spleen occured more rapidly.

The damage to the bone marrow in the animals which underwent the preliminary effect of vibration was the same as for the animals irradiated with protons, but the restoration of the bone-marrow hemopoiesis was observed during earlier periods, particularly in the case of the effect of vibration one day before irradiation.

For the effect of vibration 3 days after proton irradiation, we observed an acceleration of the destruction in the lymphoid tissue of the spleen, and also found a delay in their recovery. The myelopoeisis in the spleen was recovered earlier. The damage to the bone marrow was also intensified, and the recovery of the hemopoietic elements in it occurred less intensely than for only one irradiation with protons.

The most serious injuries to the hemopoietic organs were found for the effect of vibration 5 days after irradiation. In the spleen and bone marrow of the animals which were irradiated after the vibration, we observed an intensification of the devastation in the stroma and an additional destruction of the hemopoietic elements. The recovery of the cellular composition was made more complicated by the appearance of large-scale foci of necrosis in the spleen and bone marrow.

In those cases when the animals were subjected to accelerations one day before γ-irradiation, the destruction of lymphocytes in the follicles (and of megakaryocytes in the pulp of the spleen) decreased, and there was a certain acceleration in the recovery of the structure of the hemopoietic organs. The effect of an acceleration on the first day after the irradiation did not substantially change the radiation damage to the hemopoietic organs. /366

In comparing the morphological changes in the hemopoietic organs during the complex effect of protons and vibrations with the changes in the same organs during the complex effect of γ-rays and accelerations, we could never explain the differences found by the difference in the types of incident radiation, since the effects of the protons and γ-rays do not show a significant difference in the qualitative relationship. The explanation should be found primarily in the varying effect of the dynamic factors themselves.

In comparing the morphological changes occurring in the spleen and bone marrow after the effect of vibration and acceleration, certain qualitative differences are made clear. Thus, in the case

of the vibration, we observed a more accelerated maturation of the granulocytes in the bone marrow, i.e. stimulation of the myeloblastic growth. At the same time, in the case of the effect of acceleration, some animals showed signs of stimulation of the erythroblastic growth. Under the influence of acceleration, hypoxia of the hemopoietic organs (as a stimulation of erythropoiesis) develops as a result of a disorder in the hemodynamics [6, 7]. The vibration, which is associated with venous stasis and hemorrhages in the bone marrow (which are obviously also accompanied by hypoxia) also have a specific effect on the nuclei of the cells in the bone marrow. This effect is evidenced by the increase in the quantity of cells with chromosome changes [10]. These differences in the mechanism of the effect of the dynamic factors on the hemopoietic organs can cause the difference in the reactions of the bone marrow and spleen of the irradiated animals to the effects of vibration and acceleration.

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THE REACTIVITY CONDITION OF AN ORGANISM DURING THE COMPLEX EFFECT OF SEVERAL SPACE-FLIGHT FACTORS+

V.V. Antipov, B.I. Davydov, E.F. Panchenkova, P.P. Saksonov, and G.A. Chernov

ABSTRACT: The results presented in the article show that the dynamic factors of a flight substantially change the reaction of an organism to the effect of ionizing radiation. In this case, the directionality and magnitude of the changes depend on the nature and force of the stimulus, the time, and the sequence for the effect of the factors, the type of object, etc. The opinion is given that these facts should be considered in establishing the maximum-tolerable doses of radiation for the crew members of the craft, and in developing methods and means of counterradiation protection for the biological objects which are involved in the ecological complex.

One of the problems in space biology and medicine which require /367
comprehensive experimental studies is the problem of the effect on an organism of ionizing radiation in combination with the dynamic factors of flight. We know from the literature that such dynamic factors as acceleration and vibration can change the reactivity of an organism very substantially, leading to a change in its reaction to the effect of pharmacological preparations [1, 2], physical stress [3], and ionizing radiation [4-6].

The purpose of this article is to examine the experimental results, for radiation, of the effect of vibration or acceleration on the course and the end result of radiation sickness (the reaction to it) in animals. We also attempted to determine the possible pathways and mechanisms for a change in an organism's radiation resistance when it is affected by dynamic flight factors.

Under actual flight conditions, the dynamic factors can act on an organism either before or after the possible effect of ionizing radiation. In relation to this, we examined the effect on animals of dynamic factors and radiation in various combinations: the /368
irradiation either preceded the acceleration or vibration, or it was imposed after the effect of these factors.

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The values for the doses of penetration radiation, the parameters of the vibrational effect and acceleration, and the times between the effect of the dynamic factors and the ionizing radiation were determined, on the one hand, by our desire to make the laboratory experiment very close to the conditions of a space flight, and, on the other hand, by the type of biological object and the possibilities of the method.

The experiments were performed on 1400 male mice of no particular strain, 360 mice of the SVA strain, 120 rats, and 20 dogs.

The examinations were conducted with various types of radiation (γ-rays, X-rays, and high-energy protons).

The animals were irradiated with Co^{60} ("Khizotron" apparatus) or on a RUM-11 X-ray apparatus in doses of 400-900 r. The conditions for irradiation with the RUM-11 were the following: 180 kV, 10 mA, Al - 1.0 mm, Cu - 0.5 mm. The dose rate for the X- and γ-radiation was 13-15 r/min. Some of the animals were irradiated with protons in a dose of 1300 rad. The irradiation was accomplished in a pulsed beam of the OIYaI synchrocyclotron at Dubna, at a current density of 10^8-10^9 protons per 1 $cm^2 \cdot sec^{-1}$. The energy of the protons was 660 MeV.

Thirty minutes, 4 hours, and 1 day before (or after) the irradiation, the animals were subjected to the effect of an acceleration (or vibration). The acceleration was produced in a centrifuge with a radius of 4.25 m, and the vibration was created on a special laboratory vibration-stand. The parameters for the acceleration were 8-10 g for 15-30 min, and those for the vibration were 70 or 700 Hz for 60 min; the values for the amplitude were 0.5 and 0.005 mm, respectively.

The injurious effect of the complex of flight factors (vibration, acceleration, ionizing radiation) was evaluated with the aid of clinical-hematological, physiological, biochemical, morphological, and cytogenetic methods.

THE EFFECT OF ACCELERATION AND IONIZING RADIATION[1]

The experiments were performed on mice, rats, and dogs. The effect of the acceleration on radiation damage in the animals was determined according to the change in the fatality rate, the average lifespan, the weight of the animals during a 30-day observation, the change in the weight of the thymus and spleen, and certain hematological (quantity of leukocytes, erythrocytes, hemoglobin) and morphological characteristics.

[1]These data were obtained with the cooperation of N.I. Konnova.

TABLE 1. SURVIVAL RATE AND AVERAGE LIFESPAN FOR MICE, SHOWING THE EFFECT OF AN ACCELERATION (8-10g, 20-30 min) OR VIBRATION (70 Hz, 60 min) BEFORE IRRADIATION. /369

Groups	No. of Animals	No. of Survivors	Survival Rate, %	Average Duration, days
400 r	30	23	78 ± 7.8	11.7 ± 2.3
Acceleration + 400 r (Interval of 4 hours)	30	26	87 ± 6.2	12.7 ± 4.5
700 r	20	6	30 ±10.2	22.0 ± 1.9
Acceleration + 700 r (Interval of 30 min)	20	9	45 ±11.4	15.4 ± 1.3
700 r	30	7	23 ± 7.8	23.3 ± 1.6
Acceleration + 700r Interval of 4 hours)	30	12	40 ± 8.9	11.1 ± 1.5
750 r	173	21	12 ± 2.4	8.7 ± 1.1
Acceleration + 750 r (Interval of 4 hours)	20	7	35 ±10.6	6.4 ± 0.8
Acceleration + 750 r (Interval of 1 day)	117	25	21 ± 4.2	7.5 ± 0.4
900 r	20	0	0	10.2 ± 0.4
Acceleration + 900 r (Interval of 4 hours)	20	1	5	9.5 ± 0.6
Acceleration + 900 r (Interval of 1 day)	20	1	5	15.4 ± 1.4
1300 rad (Protons)	30	0	0	15.4 ± 0.6
Accelerations + 1300 rad (Interval of 1 day)	30	0	0	15.5 ± 1.0
375 r	58	54	89.9 ± 3.9	23.3 ± 2.5
Vibration + 375 r (Interval of 30 min)	20	13	65 ±10.6	24.8 ± 0.6
Vibration + 375 r (Interval of 4 hours)	20	20	100	30
Vibration + 375 r (Interval of 1 day)	20	17	90 ± 6.7	27.5 ± 0.2
Vibration + 750 r (Interval of 4 hours)	40	10	25 ± 6.8	12.0 ± 1.2
Vibration + 750 r (Interval of 1 day)	100	19	19 ± 3.9	9.1 ± 0.4
900 r	19	2	11.6± 7.3	14.7 ± 1.7
Vibration + 900 r (Interval of 2 hours)	10	0	0	9.5 ± 0.3
Vibration + 900 r (Interval of 1 day)	10	0	0	5.8 ± 0.8
1300 rad (Protons)	30	0	0	15.4 ± 0.6
Vibration + 1300 rad (Interval of 1 day)	30	2	7	19.3 ± 1.2

The experiments conducted showed that the preliminary effect of an acceleration 30 min or 24 hours before the irradiation in doses of 700-750 r decreased the fatality rate from the ionizing radiation, on the average, by 15-23% in comparison with the controls (the animals which were only irradiated) (Table 1, Fig. 1). In this case, we should note that we did not observe intensification of the radiation effect in any experiments of this series.

At higher doses of γ- and X-rays (900 r) and proton radiation (1300 rad), the "protective" effect of the accelerations did not appear. /370

Centrifuging the animals after irradiation also slightly increased (by 8-12%) the survival rate of the experimental animals, in comparison with the controls (Table 2).

In the experimental and control groups, the greatest fatality rate for the animals was during the period from the 3rd to the 12th day after the irradiation. After the 13th day, in the group which was subjected to the combined effect of acceleration and irradiation, the animals stopped dying, while in the group of animals which had merely been irradiated, it continued up to the 24th day.

The average lifespan of the animals which finally died after the combined effect of acceleration and irradiation in doses of 400 and 900 r was the same as for the controls, while it was 30-50% lower than for the mice which were merely irradiated (controls) at doses of 700-750 r. The average weight of the experimental mice differed little from the weight of the controls; there was only a slight decrease from the 3rd to 7th days after irradiation.

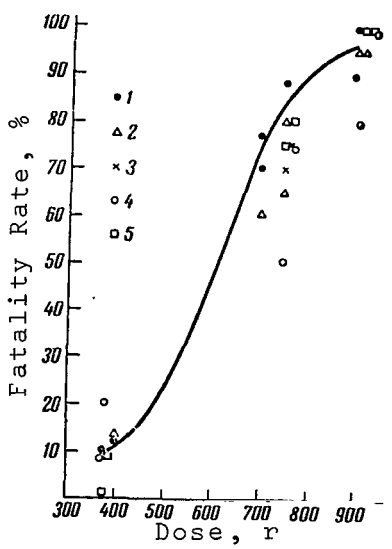

Fig. 1. Dose-Effect Curve (Fatality Rate). (1) Irradiation; (2) Acceleration + Irradiation; (3) Irradiation + Acceleration; (4) Irradiation + Vibration; (5) Vibration + Irradiation.

In the experiments on the mice of the SVA strain, we examined the change in the weight of the thymus and spleen, as well as the quantity of leukocytes, erythrocytes, and hemoglobin in the blood. The irradiation was given in a dose of 400 r, and the acceleration was 10 g for 30 min. The animals were placed in the centrifuge before and after the irradiation. The interval between the effects

was 24 hours.

We can see from the materials presented in Table 3 that in the animals which were subjected to centrifuging before irradiation, the number of leukocytes was somewhat higher than in the animals which underwent irradiation alone. In the group of mice which were placed in the centrifuge after irradiation, the number of leukocytes was somewhat higher than in the controls (Table 3). The centrifugins did not greatly affect the dynamics of the changes in the quantity of erythrocytes and the percentage of hemoglobin for the irradiated animals. The differences between the experimentals and the controls

TABLE 2. SURVIVAL RATE AND AVERAGE LIFESPAN OF IRRADIATED MICE, WITH THE SUBSEQUENT EFFECT OF VIBRATION (70 Hz, 60 min) AND ACCELERATION (10 g, 30 min) /371

Group	Number of Animals		Survival Rate, %	Average Duration, days
	Total	Survivors		
375 r	58	54	89.9 ± 3.9	23.0 ± 2.5
375 r + Vibration (Interval of 4 hours)	20	18	90 ± 6.7	23.0 ± 8.4
375 r + Vibration (Interval of 1 day)	20	16	80 ± 8.9	29.2 ± 0.3
750 r	173	21	12 ± 2.4	8.7 ± 1.1
750 r + Vibration (Interval of 4 hours)	19	9	48 ± 11.5	8.3 ± 1.2
750 r + Vibration (Interval of 1 day)	113	16	15 ± 3.3	8.8 ± 0.4
900 r	19	2	11.6 ± 7.3	14.7 ± 1.7
900 r + Vibration (Interval of 4 hours)	10	0	0	7.6 ± 0.4
900 r + Vibration (Interval of 1 day)	10	2	20 ± 12.6	8.2 ± 1.3
750 r + Acceleration (Interval of 4 hours)	20	6	30 ± 10.2	7.7 ± 1.6
750 r + Acceleration (Interval of 1 day)	74	15	20 ± 4.6	6.0 ± 0.4

for these characteristics were statistically unreliable.

It is well known that irradiation causes a decrease in the weight of the spleen and the thymus. In our experiments on the mice of the SVA strain, the weight of the thymus decreased by 50-80% on the 3rd to 7th days after irradiation, and that of the spleen decreased by 60-80%. On the 15th day after irradiation, the weight of the thymus and spleen was either near the norm or was higher than in the controls. Acceleration before or after irradiation did not affect the radiation-induced changes in the weight of the thymus and spleen (Tables 4 and 5). However, it is interesting to

TABLE 3. CHANGE IN THE NUMBER OF LEUKOCYTES (IN THOUSANDS) IN MICE, FOR THE EFFECT OF ACCELERATION (10 g, 30 min) OR VIBRATION (700 Hz, 60 min), BEFORE AND AFTER X-RAY IRRADIATION (400 r).

Group**	Before Irradiation			After Irradiation		
	Time Aft. Effect, days			Time Aft. Irradiation, days		
	3	7	15	3	7	15
Intact Animals	8,81±0,70	6,65±1,20	10,88±1,70	10,04±0,98	10,04±1,15	11,8±2,4
Irradiation	0,72±0,24	0,64±0,14	2,12±0,3	2,21±0,80	2,64±0,80	5,65±0,93
Acceleration	8,62±0,94	7,46±0,56	5,04±0,28	13,1±0,70	17,0±3,75	18,2±3,00
Vibration	13,27±1,31	7,24±0,33	11,02±1,33	10,28±0,88	11,00±1,85	9,57±1,29
Acceleration + Irradiation	1,17±0,53	1,60±0,80	3,08±0,42	1,56±0,65	0,90±0,30	6,80±1,70
Vibration + Irradiation	0,56±0,11	0,66±0,12	3,35±1,73	1,06±0,41	0,33±0,16*	4,45±0,56

*$d < 0.05$, in relation to the radiation control.

**Thirty mice in each group

TABLE 4. WEIGHT OF THE THYMUS AND SPLEEN (in mg) WITH THE EFFECT OF VIBRATION (70 Hz, 60 min) AND ACCELERATION (10 g, 30 min) BEFORE X-RAY IRRADIATION IN A DOSE OF 400 r. /372

Groups	Thymus			Spleen		
	Days After Irradiation					
	3	7	15	3	7	15
Intact Animals	49,1±0,9*	36,5±1,7	47,5±2,5	93,7±12,7	85,1±5,6	82,6±2,2
Vibration	43,3±3,9	48,4±3,5	38,9±3,8	92,3±5,1	86,7±1,7	87,9±4,8
Acceleration	48,7±2,5	37,8±1,9	36,5±2,3	91,4±5,1	75,1±3,2	84,6±3,6
Irradiation	9,2±0,7	19,7±1,4	36,4±1,5	26,5±1,7	32,5±1,8	144,7±16,2
Vibration + Irradiation	9,9±0,1	20,1±1,6	31,3±1,8	31,9±1,2	32,6±3,5	189,0±20,4
Acceleration + Irradiation	9,4±1,5	19,6±2,1	33,0±2,2	37,2±6,9	32,2±4,1	112,1±14,6

*Average Value ± Standard Error

note the differences in the variation coefficients for the animals, for the effect of acceleration before irradiation, and for irradiation alone (Fig. 2). The variation coefficient for the combined effect was higher than for the irradiation alone. For example, on the third day after the acceleration, the variation coefficient for the weight of the thymus was 45.0%, while that for the spleen was 85.5%; these values were 21.8% and 19.3%, respectively, for irradiation alone.

TABLE 5. WEIGHT OF THE THYMUS AND SPLEEN (in mg) FOR THE EFFECT OF VIBRATION (700 Hz, 60 min) AND ACCELERATION (10 g, 30 min) AFTER X-RAY IRRADIATION IN A DOSE OF 400 r. /373

Group	Thymus, mg			Spleen, mg		
	Days After Irradiation					
	3	7	15	3	7	15
Intact Animals	48,9±3,12	41,6±3,82	37,4±1,69	71,7±2,69	89,4±11,57	118,0±7,56
Irradiation	20,5±4,07	32,0±2,27	26,4±2,62	35,9±5,19	42,1±2,98	156,0±24,11
Irradiation and Vibration	15,1±1,31	32,3±4,52	33,1±1,66	31,8±4,62	35,1±2,93	114,7±12,68
Irradiation and Acceleration	18,5±3,88	33,0±2,35	22,6±3,36	34,1±4,09	40,0±6,86	140,0±26,04

The results of the morphological examination of the spleen and bone marrow of the mice which were subjected to the complex effect of the acceleration (10 g, 30 min) and the irradiation in a dose of 700 r are very interesting.[2]

Thus, on the first to third days after the effect of these factors (the acceleration was imposed one day before the irradiation), we found a greater percentage of lymphocytes (in comparison with the controls) in the follicles of the spleen in the experimental animals, and single figures of mitosis were recorded. On the 7th day, we also found megakaryocytes in the pulp of the spleen of these animals. In the spleen of the control mice, the damage was less pronounced; by the third day, the mitotically dividing cells had disappeared completely, and there were no megakaryocytes on the 7th day. All this indicates that, for the combined effect of acceleration and ionizing radiation, there was a slower destruction of the lymphocytes in the follicles than in the case of irradiation alone.

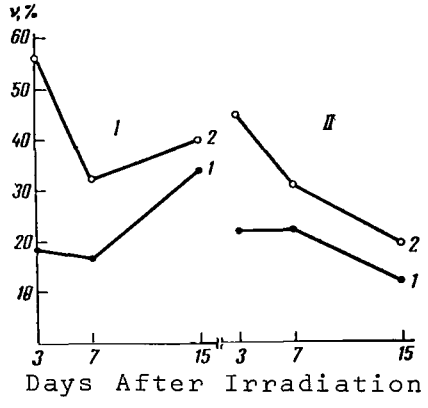

Fig. 2. Variation Coefficient (ν, %) for the Weight of the Spleen (I) and Thymus (II) After Irradiation. (1) Irradiation; (2) Acceleration + Irradiation.

On the basis of examinations of the bone marrow, we can conclude that the preliminary effect of an acceleration (1 day before irradiation) did not greatly change the destruction processes occurring in the bone marrow after irradiation alone.

[2]These studies were conducted by the authors in conjunction with N.A. Gaydamakin and V.G. Petrukhin [6].

In regard to the effect of acceleration after irradiation, the differences in the structure of the spleen (in comparison with the controls) were unimportant during all the observation periods. There were also no substantial changes detected in the morphological picture of the bone marrow, either during the period of destruction of the hemopoietic tissue, or during the recovery period.

In the experiments on rats, we examined the effect of single and repeated accelerations combined with a γ-irradiation in a dose of 600 r. The animals were placed in the centrifuge one day before /374
the irradiation. We examined the peripheral blood for its content of leukocytes in 10 rats of each group (Table 6).

TABLE 6. CHANGE IN THE NUMBER OF LEUKOCYTES (in thousands) FOR RATS, FOR THE COMBINED EFFECT OF γ-IRRADIATION, VIBRATION (70 Hz, 60 min), OR ACCELERATION (10 g, 30 min).

Group*	Original Data	Time after the Effect, days			
		1	3	7	15
Control	18,1±1,8	16,4±1,4	23,2±4,31	16,2±4,1	17,8±2,1
650 r	17,5±1,8	10,8±3,33	—	3,7±1,8	17,6±4,3
Vibration + 650 r	18,1±2,01	7,1±1,36	1,1±0,16	1,3±0,36	13,8±2,1
600 r	10,7±1,1	4,8±0,6	1,6±0,4	4,1±0,8	16,7±1,8
Acceleration + 600 r	10,3±1,5	4,7±0,7	1,1±0,4	4,9±2,0	14,2±2,0

*Ten Animals in Each Group

The results showed that there were no statistically reliable differences obtained in the survival rate and the average lifespan of the animals, although the survival rate was somewhat lower for the combined effect than for the irradiation alone; the average lifespan, on the other hand, was somewhat longer. The decrease in the number of leukocytes appeared even on the first day; this appeared to the greatest degree for the group in which the animals underwent the stress in the centrifuge before irradiation. The recovery of the number of leukocytes was somewhat delayed for the animals of this group (Table 6).

In the experiments on dogs, the complex effect of the acceleration (8 g, 3 min) and irradiation (100 r) was evaluated with the aid of certain hematological tests, as well as by the changes in the percentage of serotonin and the activity of the ceruloplasmin. The interval between the effects in these experiments was equal to 2 hours, or one day.

Figure 3 shows the average data for the changes in the number of leukocytes, expressed as a percentage of the original value. As we can see, for the animals which underwent the combined effect of acceleration and irradiation, the leukopenia was more intense than for the dogs which were only irradiated. The lowest level for the

number of leukocytes was found in the group where the interval between the effects lasted 2 hours. The recovery of the quantity of leukocytes for the dogs in the experimental groups occurred more slowly than in the controls. Thus, for the control animals, the percentage of leukocytes reached the original level around the 15th day, while it reached that level only around the 30th to 37th days for the dogs of the experimental groups. We should emphasize the fact that there was a definite correlation between the hematological/375 changes and the changes in the percentages of serotonin and ceruloplasmin for the combined effect of acceleration and irradiation.

The results of these studies were given in great detail in an article presented at the XVth Congress of the IAF [8], and will not be repeated in this article.

Thus, an analysis of the experimental materials obtained shows that the effect of an acceleration decreases the radiation damage in mice, while it intensifies certain radiation effects in rats and dogs. The modification of the radiation effect in the experiments examined above is probably linked with the change in the organism's reactivity to this factor when it is affected by an acceleration; the effect depended to a great degree on the type of animal.

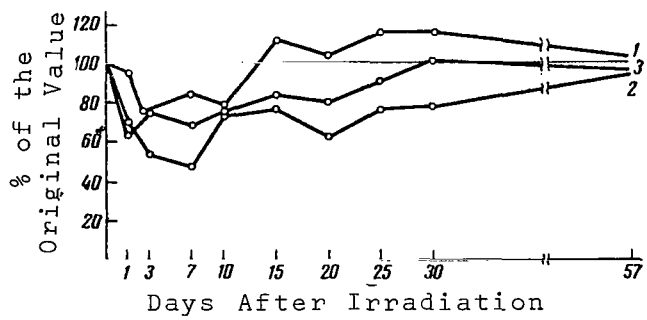

Fig. 3. Percentage of Leukocytes in the Blood of Dogs during the Combined Effect of Acceleration (8 g, 3 min) and γ-Radiation (100 r). (1) Control, for Irradiation Alone; (2) Acceleration, 2 Hours Before Irradiation; (3) Acceleration, 1 Day Before Irradiation.

THE EFFECT OF VIBRATION AND IONIZING RADIATION[3]

The experiments were conducted on mice, rats, and dogs. In order to evaluate the effect of vibration on the radiation damage, we used the same tests as in the preceding series of experiments.

The experiments showed that preliminary vibration of the mice, 4 hours and 1 day before the irradiation in doses of 375-750 r

[3]The data were obtained in cooperation with T.S. L'vova.

(X-rays, γ-rays) and 1300 rad (protons) decreased the fatality rate by 10-20%, and increased the average lifespan of the animals which eventually died by 10-40%, in comparison with the controls (the animals which were only irradiated) (Table 1, Fig. 1). In this case, we did not observe any differences between the weight of the experimental and control mice.

An increase in the radiation dose led to a change in the effect of the vibration. Thus, for the combined effect of vibration and irradiation in a dose of 900 r, the average lifespan for the animals which eventually died was less than for those subjected to irradiation alone. /376

The vibration imposed 4 hours and 1 day after X-ray irradiation in a dose of 750 r decreased the fatality rate by 6-39%, and it did not change the average lifespan of the animals in comparison with the controls (Table 2). For irradiation in doses of 375 and 900 r, the vibration did not affect the dynamics of the radiation damage. However, the average lifespan for the combined effect of vibration and irradiation in a dose of 900 r was less (in relation to statistical reliability; $d < 0.001$) than for the irradiation alone.

In the mice of the SVA strain, we examined the dynamics for the weight of the spleen and thymus, and also determined the quantity of leukocytes, erythrocytes, and hemoglobin. The irradiation was imposed in a dose of 400 r (γ-rays); the animals were subjected to the vibration once, before or after the irradiation. The vibration frequency was 700 Hz, the time for the effect was 60 min, and the interval between the vibration and the irradiation was one day. The results of this experiment are given in Tables 3 to 5. As we can see from the data presented, the quantity of leukocytes was less for the combined effect of the vibration and irradiation than for the irradiation alone. On the seventh day after the irradiation, these differences were statistically reliable ($d < 0.05$) in the group where the animals underwent vibration after irradiation.

The vibration had no substantial effect on the radiation-produced changes in the quantity of erythrocytes and the percentage of hemoglobin.

The vibration effect before the irradiation, or after it, did not affect the radiation-produced changes in the weight of the thymus and spleen.

Let us examine briefly the results of the morphological examinations of the spleen and the bone marrow in the mice which were subjected to the complex effect of vibration and high-energy protons [6].

The effect on the animals of vibration which was imposed one day before the proton irradiation (dose of 820-860 rad) resulted

in the preservation of a rather large quantity of cells with myeloid hemopoiesis in the spleen and bone marrow, in comparison with the hemopoietic organs of the control animals. At the same time, the preliminary effect of vibration before irradiation intensified the disintegration of mature cells of lymphoid type in the follicles and pulp of the spleen. With a combined effect of vibration and radiation, the erythroblasts in the bone marrow were preserved in rather greater numbers, and their restoration occurred more rapidly after the irradiation than for irradiation alone.

In the experiments on the rats, we examined the effect of a vibration (single and repeated four times) of 70 Hz for 60 min, in combination with γ-irradiation in a dose of 650 r. The animals underwent the vibrations one day before the irradiation. In order to calculate the number of leukocytes, we examined the peripheral blood of 10 rats in each group (Table 6).

As the experiments showed, the preliminary effect of a single vibration and a vibration repeated four times before irradiation, increased the fatality rate although the vibration repeated four /377
times somewhat increased the average lifespan for the animals which eventually died. The quantity of leukocytes in the experimental groups was smaller than in the controls. Around the 15th day, the quantity of leukocytes reached the original level for the control group, while this was not noted in the experimental group. The decrease in weight was the same for the combined effect as for the irradiation alone.

In the experiments on dogs, we examined the hematological changes, the serotonin content, and the activity of the ceruloplasmin, for the effect of vibration (70 Hz, 60 min) before γ-irradiation in a dose of 100 r. The interval between the vibration and the irradiation was 2 hours or 1 day.

With the effect of vibration before irradiation, the quantity of leukocytes was greater than in the controls with irradiation alone. This intensification was noted most clearly during the 2-hour interval between the effects (Fig. 4). The changes in the serotonin content and the activity of the ceruloplasmin in the blood of the dogs were different for the combined effect of

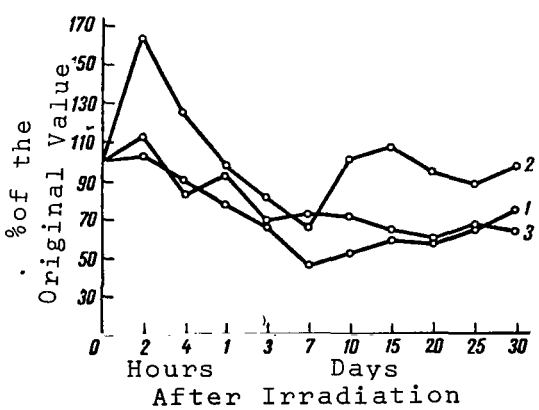

Fig. 4. Quantity of Leukocytes in the Blood of Dogs; Combined Effect of Vibration (70 Hz, 60 min) and γ-Radiation (100 r). (1) Irradiation; (2) Vibration, 2 Hours Before Irradiation; (2) Vibration, 1 day Before Irradiation

the vibration and irradiation, and for the irradiation alone, which agrees to a considerable extent with the histological changes [10].

As we can see from the above-mentioned experiments on mice and dogs, the radiation pathology for the combined effect of vibration and irradiation was less pronounced than for the irradiation alone. This "protective" effect was expressed in the decrease of the fatality rate, the increase of the average lifespan for the animals which eventually died (the experiments on mice), and the reduced decrease in the quantity of leukocytes (the experiments on dogs). /378
The results obtained for the mice and dogs do not coincide with the data obtained for rats. In the latter, there were more pronounced radiobiological effects for the combined action of vibration and irradiation. Therefore, vibration, as well as acceleration, changes the reactivity of an organism to the radiation factor in various ways, depending on the type of animal.

DISCUSSION

In the combined effect of the dynamic flight factors and radiation, the latter is the dominant factor in the injurious effect on an organism; we therefore selected tests which characterized the effect of ionizing radiation: survival rate, average lifespan, dynamics for the body weight and the weights of the spleen and thymus, hematological characteristics, and morphological changes in the spleen and bone marrow.

We attempted to sum up the results of the experiments conducted, as well as the data in the literature, in the form of alternate indices (Fig. 5). Having analyzed the results presented in this figure, we should point out the following circumstance: with the effect of acceleration or vibration before irradiation, there was a weakening of the radiation effect in 10 out of 17 and 11 out of 17 indices, respectively.

It is very difficult at the present time to give an exhaustive explanation for the modifying effect of vibration and acceleration on the radiation effects in various types of biological objects. In the animals, we suggest the following mechanism for the reduction of radiation injuries by the preliminary effect of vibration and acceleration.

Acceleration, in addition to other effects, ultimately causes hypoxia of the tissues in various organs including the hypothalamic region, which regulates the endocrine glands. It was also found that accelerations result in an increase of the histaminase, adrenalin, and noradrenalin in the blood [8, 13, 14, 16]. Vibration affects all the tissues and cells of an organism and can lead to activation of the endocrine glands. These changes in an organism can be one of the causes for the increase in the organism's resistance to ionizing radiation after the effect of the dynamic flight factors. It is well known, for example, that the intensification

of the functional activity in the adrenal cortex before irradiation, caused by administering salicylates, an adrenocorticotropic hormone, or desoxycorticosterone acetate, increases the resistance of the animals to general irradiation [15].

The data obtained in a cytogenetic and morphological examination of the hemopoietic organs of mice which were subjected to the effect of the dynamic factors [4, 6, 11, 12] are also of definite interest for an explanation of the modifying effect of vibration and acceleration on the radiation reaction. It was clearly shown in these studies that both vibration and acceleration produce (for example) a decrease in the mitotic activity of the cells in the bone marrow and spleen, and cause formation of chromosome adhesions, which is admittedly an advantageous effect for the course and end result of radiation damage. /379

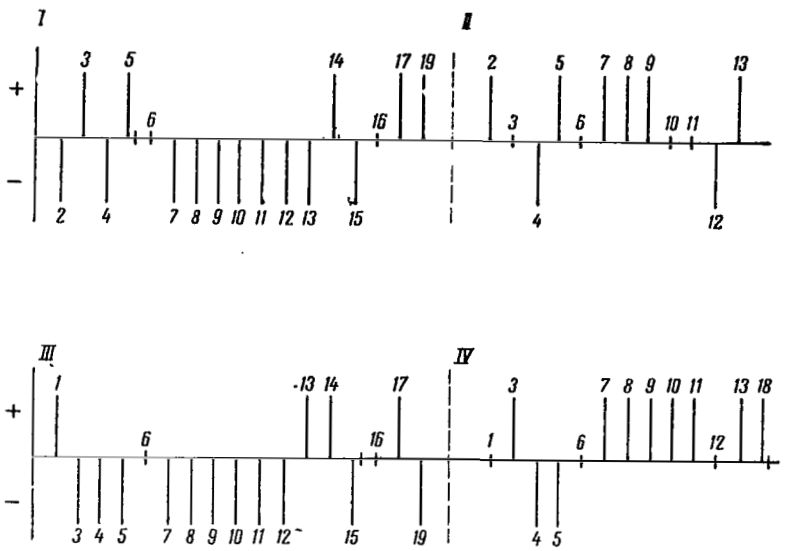

Fig. 5. Changes in Individual Indices for the Combined Effect of Acceleration, Vibration, and Irradiation. (I) Acceleration + Irradiation; (II) Irradiation + Acceleration; (III) Vibration + Irradiation; (IV) Irradiation + Vibration; (1) E. coli (Phage Production); (2) Tradescantia Paludosa (Chromosome Rearrangements); (3) Drosophila Melanogaster (Frequency of Appearance of Crosses); Mice: (4) Fatality Rate; (5) Average Lifespan; (6) Body Weight; (7) Weight of the Spleen; (8) Weight of the Thymus; (9) Number of Leukocytes; (10) Morphological Picture of the Bone Marrow; (11) Morphological Picture of the Spleen; (12) Chromosome Rearrangements in the Cells of the Bone Marrow; (13) Chromosome Adhesions in the Cells of the Bone Marrow; (14) Fatality Rate (Rats); (15) Average Lifespan (Rats); (16) Body Weight (Rats); (17) Quantity of Leukocytes (Dogs); (18) Morphological Picture of the Organs (Mice); (19) Quantity of Leukocytes (Dogs); (±) Intensification and Weakening of the Radiation Effect.

Because of a lack of experimental data, an explanation of the mechanism for the intensification of the radiation damages by the effect of the dynamic factors is even more difficult. It is very obvious that this aspect of the problem, concerning the complex effect of ionizing radiation and other flight factors on an organism, /380 awaits an experimental solution.

Obviously, the mechanisms for the modifying effect of vibration and acceleration on radiation damage in animals are varied. This is indicated, for example, by the data on the change in the serotonin content and the activity of the ceruloplasmin in the blood, for a combined effect of acceleration with irradiation, and vibration with irradiation. In the first case, both the serotonin content and the activity of the ceruloplasmin change; in the second, only the activity of the ceruloplasmin changes. The results obtained from an examination of animals' resistance to physical stress after the effect of an acceleration or vibration also indicate that these factors cause various changes in the reactivity of an organism.

Therefore, an analysis of the materials obtained shows that the dynamic flight factors substantially change the reaction of an organism to the effect of ionizing radiation. The directionality and magnitude of the changes depend on the nature and force of the stimulus, the time, and the sequence of the effect of the factors, the type of subject, etc. Obviously, these facts must be considered in finding solutions to a number of problems related to the practice of space flights: for example, in establishing the maximum-permissible levels of radiation for the crew members of the craft, as well as in developing methods and means for counterradiation devices for various biological subjects which are included in the complex of the ecological system.

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RELATIVE BIOLOGICAL EFFECTIVENESS AND PICTURE OF RADIATION DAMAGE UNDER THE INFLUENCE OF IONIZING RADIATIONS WITH VARIOUS VALUES FOR LINEAR LOSSES OF ENERGY

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ABSTRACT: The article gives experimental data on the biological effectiveness of ionizing radiations which vary in LLI (linear losses of energy). A congruity was established in the general picture for severe radiation damage caused by the effect of isoequivalent ionizing radiations which differ in LLE, particularly in the degree of injury to the hemopoietic organs. However, the RBE (relative biological effectiveness) coefficients of various ionizing radiations for severe damage cannot be used for evaluating the biological effect of radiation when the remote aftereffects of radiation sickness are of primary importance.

The development of space research poses the problem of guaranteeing protection against radiation during space flights [2, 4, 15, 32]. /381 In relation to this, the problem of the relative biological effectiveness of various ionizing radiations is particularly timely, since an evaluation of the biological effect of mixed fluxes of various radiations, characteristic of space radiation, must be based on a knowledge of the quantitative rules for the ratio between the values for the linear losses of energy (LLE) and the relative biological effectiveness (RBE) of the ionizing radiation. Most ionizing radiations of a cosmic nature have small LLE values, roughly on the same order as X-rays or γ-rays [3]. However, in the case of large irradiating objects, and particularly irradiations beyond barriers with insufficient power, it is possible that there will be dosage bands whose energy spectrum is "blurred" over a wide range of LLE values. The interest in the hard-radiation component of the cosmic radiations is also due to the presence in them of heavy nuclei with large LLE values, since the density of ionization for otherwise equal conditions is proportional to the square of the charge of the particle [20].

Moreover, we have not excluded the possibility of using nuclear reactors, whose background radiation is mainly produced by hard-radiation fluxes of neutrons, for the motors of spacecraft.

In this article, we shall provide experimental data on the /382

biological effectiveness of ionizing radiations which differ in LLE, in relation to acute symptoms of radiation sickness. Moreover, this study followed the goal of comparing the picture for radiation damage to animals during the action of various ionizing radiations, and of evaluating the possibility for developing curative processes. In examining our data and that in the literature, we also attempted to evaluate the danger of chronic exposure to ionizing radiations with various LLE values.

In the experiments, we examined the biological effect of protons of 660 MeV, γ-rays from Co^{60}, X-rays with a peak potential of 180 kV, and fission neutrons. The LLE values for the ionizing radiations used in the experiments are given in Table 1. The source for the high-energy protons was the OIYaI synchrocyclotron at Dubna. The operational methods and dosimetry in the experiments with the high-energy protons were described in great detail in earlier articles [1, 11]. The dose rate of the protons in the experiments was equal to 200-500 rad/min.

TABLE 1. LLE VALUE FOR THE VARIOUS IONIZING RADIATIONS

Type of Radiation	Average LLE Value, keV/μ
Protons, 660 MeV	0.3
γ-Rays from Co^{60}	0.3
X-Rays, 180 kV	3.0
Fission Neutrons	30.0-50.0

The source of the fission neutrons was the Type 1BR atomic reactor at the Laboratory of Neutronic Physics in the same Institute. The average energy of the neutrons was 0.3-0.4 MeV, caused by the presence of a neutron moderator along the path of the beam. The dose rate of the neutrons, under various conditions, was 60-400 rad/hour. The source of the γ-rays was the GUT-Co-400 apparatus which provided irradiation at a dose rate from 40 to 100 rad/min. The source of the X-rays was the RUT-3-20-200 apparatus which operated under the standard conditions (potential of 180 kV, current strength of 15 ma, 0.5 mm filters of Cu and 1.0 mm of Al, focal length of 38 cm, dose rate of 30 rad/min). For the biological subjects in the experiments, we used yeast cells of two types: haploids of Zygosaccharomyces cerevisae and diploids of Saccharomyces vini. The animals used were mice, rats, and rabbits.

The first series of experiments involved an examinations of /383
the relative biological effectiveness of various ionizing radiations in relation to the radiation damage to the yeast cells. The types of yeast cells used in these experiments have been thoroughly studied in terms of their radiobiological relationship [12, 13]. The survival rate of the irradiated yeast cells was examined by the method for calculating microcolonies [13], which allowed considering

the distribution of inactivated cells by the shapes of the microcolonies, in addition to the general survival rate of the cells. The dosage curves for inactivation of the haploid type have an exponential form for all the types of radiation, while those for the diploid type have an S-shape. The values of the LD_{50}, calculated from the experimental data, are given in Table 2. These values were used for calculating the RBE coefficients of the ionizing radiations.

TABLE 2. RELATIVE BIOLOGICAL EFFECTIVENESS OF VARIOUS IONIZING RADIATIONS, CALCULATED ACCORDING TO THE DATA FOR THE SURVIVAL RATE OF THE IRRADIATED YEAST CELLS

Indices		Protons, 660 MeV	γ- Rays Co^{60}	X-rays	Fission Neutrons
LD_{50}	Haploid	5.3±0.6	5.3±0.3	4.0±0.5	1.9±0.3
	Diploid	29.0±2.8	29.2±1.4	25.1±3.2	-
RBE for X-rays of 180 kV.	Haploid	0.76	0.76	1.0	2.1
	Diploid	0.86	0.86	1.0	-
RBE for γ-rays of Co^{60}	Haploid	1.0	1.0	1.3	2.8
	Diploid	1.0	1.0	1.2	-

As we can see from Table 2, the effect of protons of 660 MeV and γ-rays of Co^{60} on the two types of yeast cells, calculated according to the survival rate, is identical. The distribution of the forms of microcolonies of the inactivated cells is also identical for these radiations. On the other hand, these radiations have close LLE values, which allows us to conclude that the values for the LLE have a definite role in the RBE of the ionizing radiations (this stands to reason, in view of the other factors which can modify the observed effect). A similar appearance of a congruity in the biological effectivity of the radiations produced by various sources, but producing the same density of ionization, was called a transgression by Lea et al. [11-12]. The concept of transgression plays a definite role in analyzing the interrelationships between the LLE and the RBE of ionizing radiations. With an increase in the LLE value of a radiation, the RBE values which were determined in the experiments on the yeast cells also increased. For other biological objects, a similar picture of the increase in the RBE of an ionizing radiation with an increase in the LLE values was also noted by other authors [9, 19, 22, 28, 30, 35]. Only for very high values of LLE (which usually exceed 100 keV/μ) does the value of the RBE again decrease [35]. /384

The second series of experiments, involving an examination of the RBE for the same types of radiations, was conducted on mice. The criterion for radiation damage was the death of the animals

during an acute period of radiation sickness, which was induced by various doses of radiation so that we could calculate the $LD_{50/30}$. The results of these experiments are shown in Table 3, where the RBE coefficients of the ionizing radiations were calculated according to the values of the $LD_{50/30}$. As we can see, the general character for the change in the RBE of the ionizing radiations in relation to the LLE (which was studied in experiments on isolated cells) is also observed in the test for the survival rate of the animals.

TABLE 3. RELATIVE BIOLOGICAL EFFECTIVENESS OF VARIOUS IONIZING RADIATIONS, CALCULATED ACCORDING TO THE DATA FOR THE FATALITY RATE OF THE IRRADIATED MICE

Indices	Protons of 660 MeV	γ- Rays of Co^{60} from	X-Rays	Fission Neutrons
Ld_{50}, rad	880 ± 29	795 ± 24	590 ± 21	218 ± 16
RBE for X-rays	0.67	0.74	1.0	2.7
RBE for γ-rays Co^{60} from	0.90	1.0	1.34	3.6

This is undoubtedly an indication that the survival rate of the irradiated animals is ultimately determined by the survival rate of the cells in the radiation-sensitive organs, particularly in the hemopoietic organs and the intestine [6, 33]. It is interesting to note that in cells which differ greatly from one another (isolated cells of microorganisms and cells of radiation-sensitive organs in animals, which differ in radiation sensitivity by an order of 1-2), there is a similar character observed in the ratio between the RBE and the LLE. Obviously, this shows the general character of the relationship observed.

A certain difference in the effectiveness of the protons of 660 MeV and the γ-rays from Co^{60} in terms of the fatality rate of the mice obviously can be explained by the conditions for the experiments. The proton irradiation is ultra-fractionated, with a pulse length of 200-400 μsec, and a rate of 100 pulses/sec. Therefore, the actual dose rate per pulse exceeds the average dose rate by an order of 1-2. There are experimental data which show that, for very high dose rates of ionizing radiation, there is a /385
certain decrease in its effectiveness [8, 10]. The data of this experiment also correspond well with the concepts of a transgression of the ionizing radiations. At the same time, even in irradiation of such small animals as mice, we can begin to see additional factors which could not take place in the case of irradiation of cells. In relation to the nonuniformity of the atomic composition in various animal tissues, the absorption doses in various organs can be different. Thus, according to the data of Sinclair [34], the absorption doses in the bone marrow of a mouse or rat in the case

of X-ray irradiation exceed the mid-tissular doses for soft tissues roughly by 10%; for the effect of harder radiations (γ- rays from Co^{60} or X-rays of 22 MeV), the absorption doses in the bone marrow and soft tissues are equal. This, obviously, is the cause of the fact that for X-rays the greatest relative value is found for the interval between the $LD_{100/4}$ and the $LD_{100/30}$; for the effect of γ- rays from Co^{60} or high-energy protons, the given interval decreases, as we have described in previous articles [19], and which was noted by other authors [26]. The value for the interval between the $LD_{100/4}$ and the $LD_{100/30}$ can be calculated with the aid of the criterion "*K*" which we introduced. The criterion "*K*" is equal to the ratio between these two values (Table 4).

TABLE 4. CALCULATED CONSTANTS OF "*K*" FOR MICE IRRADIATED BY VARIOUS TYPES OF IONIZING RADIATION.

Type of Radiation	$LD_{100\ 30}$, rad	$LD_{100\ 4}$, rad	*K*
Protons of 660 MeV	1000	1400	1.4
γ- rays from Co^{60}	900	1300	1.4
X-rays	700	1200	1.7
Fission Neutrons	270	300	1.1

The effect of the non-uniformity in irradiation is seen particularly in the irradiation of large animals, in relation to which we must calculate the distribution of the absorbed energy throughout the extent of the body as well as the flux of the incident radiation. A second important factor which should be considered is the irregular increase in the value of the RBE for various occurrences of a radiation effect during an increase in the LLE of the ionizing radiations. A characteristic example of such a phenomenon can be found in examining the same for Table 4. As we can see, for the fission neutrons, the value for the interval between $LD_{100/4}$ and $LD_{100/30}$ is less than for the other types of ionizing radiation. At the same time, as follows from the considerations of Alpen et al. /386 [25], such a difference could never be explained only by the irregular distribution of the absorption energy for the neutrons in the body of the animals. The average lifespan of the mice which eventually died after exposure to neutrons was less than for irradiation with equivalent doses of softer radiation. This shows the great intensity of the intestinal syndrome during the action of hard-radiation fission neutrons.

However, the injury to a number of other organs and systems during the action of various ionizing radiations at doses which are equivalent with respect to the fatality rate is roughly identical. This relates primarily to the damage to the blood and the hemopoietic organs, which we showed in the third species of experiments. This series involved a comparative evaluation of the radiation injuries and recovery for animals which were exposed to various types of radiation in isoequivalent doses. A comparison of the radiation

damage for mice, which were subjected to irradiation by protons of 660 MeV, X-rays of 180 kV, or fission neutrons, was made at three different radiation doses which were equivalent, considering the OBR coefficients equal to 300, 700, and 1500 rem. The dose of 300 rem was roughly equal to 0.5 $LD_{50/30}$, and was not fatal; the dose of 700 rem corresponded roughly to the absolute minimun lethal dose; the dose of 1500 rem led to the death of all the animals within four days after the irradiation, due to the "intestinal" variety of acute radiation sickness. The degree of radiation damage in the mice was evaluated according to the change in the weight of the body, the spleen, the small intestine, and the testis, as well as by the quantity of leukocytes and erythrocytes in the blood and the number of cells in the bone marrow in the femur.

An analysis of the results of the experiments led to the conclusion that the degree of the damage to the hemopoietic organs of the mice which were exposed to various types of ionizing radiation in doses which were equivalent in terms of the fatality rate were roughly identical. In irradiating the mice with protons of 660 MeV, X-rays of 180 kV, or fission neurons in a dose of 300 rem, related dynamics are observed for the change in the weight of the spleen and the number of cells in the bone marrow in the femur. During the first few days after irradiation, the weight of the spleen and the quantity of cells in the bone marrow decrease sharply, constituting roughly 30% of their value in the control animals. Then, as a result of a development of the regenerative processes, there is a rapid increase in the weight of the spleen and the quantity of cells in the bone marrow in the femur of the control (non-irradiated) animals. Obviously, this is a sign of "hyperfunction" of the hemopoietic system, which develops as a result of recovery from the radiation injuries. Within 25 days after irradiation in a dose of 300 rem, the irradiated and control mice do not show a reliable /387
variation in the weight of the spleen and the quantity of cells in the bone marrow. Similar dynamics for the change in the weight of the spleen and in the number of cells of the bone marrow in the femur are also found for the mice which were subjected to irradiation by various types of ionizing radiation in doses of 700 and 1500 rem. In these cases, there is a sharp decrease in the weight of the spleen and the quantity of cells in the bone marrow during the first days after irradiation, which then remains roughly the same until the death of the animals.

The weight of the body and the small intestine, as well as the quantity of leukocytes and erythrocytes in the blood, change roughly in the same way for the mice which were exposed to various types of ionizing radiation at all the doses we used in the experiments. We can only note that, in relation to the exposure of the mice to fission neutrons in doses of 700 and 1500 rem, the decrease in the weight of the small intestine during the first three days after irradiation somewhat exceeds the decrease in the weight of this organ in the case of exposing the mice to protons of 660 MeV or X-rays of 180 kV.

A reliable difference in the degree of intensity of the radiation damage in the mice which were subjected to irradiation by soft or hard radiation was observed only in the change in weight of the testes. The weight of the testes decreased more after neutron irradiation than after irradiation with protons of 660 MeV or X-rays of 180 kV in isoequivalent doses.

A comparison of the biological effectiveness of soft and hard radiation was also conducted according to a number of characteristics for acute radiation damage in rats and rabbits. In the rats which were irradiated with protons of 660 MeV or fission neutrons in doses of 300, 700, and 1500 rem, we observed characteristic changes in the hemolytic resistance of erythrocytes, calculated according to the erythrogram method. During the first several days after irradiation, there is a definite decrease in the hemolytic resistance of the erythrocytes, which obviously is related to the direct effect of the radiation on the erythrocytes. The hemolytic resistance of the erythrocytes in the irradiated animals exceeded the resistance of the erythrocytes in the control animals in certain cases; this is related to the ejection of new, "immature" cells into the blood flow. In the case of the death of the animals during the terminal period, the shape of the erythrograms was sharply deformed, which can be explained by the effect on the erythrocytes of toxic products accumulated in the organism. These could be of a lipid nature. There were no significant differences found in the nature of the change in the erythrograms for the rats which were exposed to two radiations which differed sharply in the LLE (protons of 660 MeV and fission neutrons). A similar picture for the change in the erythrograms of the rats was described earlier for irradiation by X-rays and γ-rays [4, 21], and for irradiation by fast neutrons [24].

An examination of the autolysis in homogenates of the liver /388
and spleen, in rats which were subjected to irradiation by protons of 660 MeV or fission neutrons in doses of 300, 700, and 1500 rem, showed that the change in intensity of autolysis depends on the dose of irradiation; with an increase in the dose, it takes on a pronounced phase character. During various periods after the irradiation, we can observe both acceleration and retardation of the autolytic reaction. Although there is a certain difference in the intensity and periods for a change in the autolysis of animals which were irradiated with protons of 660 MeV or fission neutrons, we nevertheless must note that the autolytic reactions for ionizing radiations which vary in LLE have the same general phase nature.

The formation and accumulation of various toxic products in the organs and tissues of irradiated animals has been shown convincingly in a number of recent studies. Obviously, among the other radiotoxins, an important role is played by the lipid toxins [14]. Therefore, the study compared the dynamics for accumulation of products with oxidation of lipids in the liver of rats, with the toxicity of the acetone fraction of the lipid excretion from the livers of rabbits which were subjected to irradiation by high-

energy protons and fission neutrons in doses which were isoequivalent according to the fatality rate. It was established that under the effect of both types of irradiation in a dose of 800 rem, there are substances in the butanol extracts from the liver of rats, which produce a specific reaction with thiobarbituric acid. This is usually considered as an indication of the presence of oxidation products of lipids [27]. The quantity of these products increases with the development of the radiation damage, and it reaches a maximum during the terminal stage of acute radiation sickness. Having evaluated the toxicity of the acetone fraction in the lipid excretion from the liver of the rabbits (which were killed on the third day after irradiation by a dose of 1000 rem) by the hemolytic test, we find that it is roughly identical for both types of ionizing radiation.

Thus, according to a large number of characteristics for radiation damage, the exposure of the animals to isoequivalent doses of various ionizing radiations leads to an identical picture for the radiation damage. Therefore, the intensity of the "intestinal" syndrome of neutron irradiation shows an increase in the LLE value for the ionizing radiation means that the RBE value for the damage to the intestine increases more rapidly than the RBE value which was calculated according to the fatality rate of the animals. Therefore, if the intestine is more radiation-resistant than the hemopoietic organs to the effect of soft radiation, and an increase in the radiation dose reveals a "bone-marrow" form of radiation damage followed by an "intestinal" form of damage to the animals, then the effect of hard radiation causes the radiation sensitivity of the intestine to decrease roughly to the level of that for the hemopoietic organs. When the mice are exposed to hard radiation, most of them die from the "intestinal" variety of acute radiation /389
sickness which does not reach the "second peak" of destruction, and the damage of the hemopoietic organs seems to be "concealed" because of the great severity of the intestinal injury. Naturally, for the effect of radiation in smaller doses, the damage to the hemopoietic organs (which determine the dynamics for the development of the restoration processes) is of primary importance. Such a conclusion was substantiated by the data from the experiments studying the rapidity of "recovery" for the mice which were subjected to irradiation by protons of 660 MeV, X-rays of 180 kV, or fission neutrons in a dose of 300 rem. After irradiation, the "remanent damage", determined by means of repeated X-ray irradiation, begins to decrease rapidly (roughly according to the exponential law) and reaches zero around the 7th to 9th days after the irradiation. During the following period, there is a condition of increased radiation-resistance, the maximum of which occurs roughly on the 12th to 14th days after irradiation. The increase in the radiation-resistance during a certain period after a non-fatal irradiation was also observed by others in similar experiments. Obviously, the increase in the radiation-resistance is connected with the "hyperfunction" of the hemopoietic system, as a result of a development of the reparative processes. By the 20th day after the irradiation,

the radiation-sensitivity of the experimental animals is almost the same as for the controls. For all three types of ionizing radiation, the differences in the dynamics for the change in the magnitude of the "remanent damage" are not reliable. The dynamics for the change in the magnitude of the "remanent damage" after the non-fatal irradiation undoubtedly reflect the dynamics for the development of regenerative processes in the hemopoietic organs. In the case of repeated irradiation by X-rays in doses at the same intervals as were used in our experiments, the survival rate is determined according to the state of the hemopoietic organs. The phenomenon of "increased radiation-resistance" observed after non-fatal irradiation is very interesting. A comparison between the duration of the increased radiation-resistance and the data on the dynamics for the change in the organs and systems of an animal after irradiation allows us to draw the conclusion that the condition of increased radiation-resistance is apparently a reflection of the condition of "hyperfunction" for the radiation-sensitive organs, primarily the hemopoietic organs.

Therefore, the results of the examinations conducted show the congruity of the general picture for acute radiation damage to animals, caused by the effect of isoequivalent ionizing radiations which vary in LLE, particularly in that part which is determined by the degree of injury to the hemopoietic organs. The quantitative interrelationships between the LLE of the ionizing radiations and the RBE, calculated according to the fatality rate of the animals, can be described in a good approximation by the following empirical formula:

$$RBE = 0.8 + 0.06 \times LLE,$$

where the value for LLE is taken as 1 keV/μ. The convenience of /390
this formula in relation to the calculations for the "biological dose" of the mixed fluxes of radiations is linked with the linear character of the relationship between RBE and LLE.

The above-described nonuniformity of the increase in the RBE for certain organs and systems of an animal (intestine, testes) with an increase in the value of the LLE for the ionizing radiations, cannot be used in the case of acute damage in calculating the biological effect of the radiation when the remote aftereffects of the radiation damage are of primary importance. These concepts relate primarily to soft-radiation, high-energy protons, which can transfer some of the absorbed energy of the radiation in the same way as for a hard radiation. For acute radiation damage caused by high-energy protons, a similar "ad-ition" of hard radiation has practically no effect, and the RBE is within the range of one unit; we must await a significant increase in the value of the RBE for the remote aftereffects of proton irradiation.

The limited data on the carcinogenic effect of protons of 660 MeV [23] seem to confirm the concepts presented here. However, it

is certain that further studies are necessary for answering this question.

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RELATIONSHIP BETWEEN THE FUNCTION OF THE THYROID GLAND AND THE CHOLINESTERASE ACTIVITY OF THE HYPOTHALAMUS, THALAMUS, PALEO-, ARCHEO-, AND NEOCORTEX IN DOGS SUFFERING FROM ACUTE RADIATION SICKNESS

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ABSTRACT: The function of the thyroid gland was examined in experiments on dogs by using the accumulation and excretion of I^{131}. The cholinesterase activity in the anterior and posterior regions of the hypothalamus, thalamus, paleocortex, archeocortex, neocortex, and cerebellum was also examined. A decrease in the accumulation of I^{131} in the dogs within 14 months after irradiation with a dose of 400 r was accompanied by a decrease in the cholinesterase activity in the hypothalamus and thalamus. A determination of the correlation coefficient according to Spearman's formula showed that the most rigid relationship ($p = +0.95$) is found between the accumulation of I^{131} and the cholinesterase activity in the hypothalamus.

An examination of the changes in the neuro-endocrine system /391
during the effect of extreme flight factors is not only of interest for space physiology, but can also shed light on certain obscure problems in motor psychology. In planning a space flight, we must consider particular features of the reaction of various structures in the cerebrum, particularly those responsible for the behaviorial reactions of an organism (hypothalamus, hippocampus, limbic cortex) /392
during the effect of flight factors. The neuroendocrine system is particularly sensitive to ionizing radiation.

A study of the regulation of the thyroid gland is of definite interest, since the metabolism and oxygen balance in organisms suffer greatly from a disorder in this gland.

Most researchers consider that the feedback system of the thyroid gland-pituitary, which controls the excretion of the thyrotropic hormone, depends mainly on the hypothalamus [1,17,25]. The thyroid gland is regulated, not only by the hypothalamus, but, obviously, by other regions in the cerebrum: the thalamus, as well as the frontal and limbic regions of the cortex, and the hippocampus [2, 10, 20,]], 25].

It was shown earlier that in dogs with acute radiation sickness, certain aspects of the metabolism of the acetylcholine in the hypothalamus and thalamus are disturbed [7,8]. On the other hand,

the function of the thyroid gland in animals is affected for 3.5-le months after radiation damage [3].

In this article, we have attempted to examine the relationship between the functional condition of the thyroid gland and the activity of the cholinesterase in the hypothalamus, thalamus, cerebellum, and phylogenetically-different cortical structures: the paleo-, archeo-, and neocortex. We determined the relationship with the aid of the correlation method.

METHODS.

The experiments were conducted on 18 male mongrel dogs, about 1.5-2 years ole at the time of irradiation. The animals were subjected to a general γ-irradiation of Co^{60} in a dose of 400 r (13 r/min). According to the data of the preliminary experiments, this dose consisted of $LD_{50/30}$. All the animals were kept on a regular diet under the same conditions. The function of the thyroid gland was examined by the absorption of I^{131} within 9-14 months after the irradiation, by using intravenous administration of I^{131} without a carrier in a quantity of 10 μC. The absorption of I^{131} by the thyroid gland was determined from the γ-radiation, with the aid of a shielded detector made up of three gas counters. The anterior surface of the animal's neck (in the region where the thyroid gland protruded) was placed at a distance of 7 cm from the detector. Each measurement lasted 3-5 min. The experiments on the control and experimental animals were conducted simulataneously. Fourteen months after irradiation, the animals were decapitated; the cerebrum was extracted, the pia mater was isolated, and a section of the optic nerve was separated. The cerebrum was then divided into two hemispheres by sagittal section and frozen in carbon dioxide. After this, we excised the hypothalamus, thalamus (mainly the central-medial nuclei) and the parts of the cortex which corresponded topographically to the following regions: the preperiform-periamygdalar region of the paleocortex, the ventral portion of the hippocampus (archeocortex), and the frontal-limbic region of the neocortex [4]. In the study, we also made a thin section of an entire hemisphere of the cerebellum. The cholinesterase activity was determined in extracts of the brain tissue by the somewhat modified spectrophotometric method of Gregoire and Limozin [21]. As a substrate for the cholinesterase, we used acetylcholine chloride in an ultimate concentration of $6.9 \cdot 10^{-4}$ M. The cholinesterase activity was expressed in micromoles of the disintegrated acetylcholine for one hour in an extract of 100 mg of fresh tissue at 25° and a pH of 7.5. /393

The experimental materials were subjected to a statistical analysis, calculating the arithmetic average and the quadratic error of the average. We determined the correlation coefficient among the individual indices according to Spearman [13].

RESULTS AND DISCUSSION

The experimental data obtained are shown in Tables 1 and 2 and Figure 1. Figure 1(A) shows the curves for the accumulation of I^{131} by the thyroid gland of a dog, 9 months after γ-irradiation. It was shown previously [3] that 50-87% of the irradiated animals showed a curve for the absorption of I^{131} with a maximum within 6-14 hours and a relatively rapid decrease. We observed such a curve in these experiments in Dogs 21 and 495 (irradiated), and in one control animal (No. 904). The amount of I^{131} accumulated by the thyroid gland, 24 hours after administration, was less for the irradiated dogs than for the control: 212 ± 90 and 260 ± 32 impulses/min, respectively ($p > 0.05$). However, if we exclude Dog No. 904 from the group of control animals, and No. 9 from the group of irradiated dogs, then the probability of a difference becomes statistically reliable ($p < 0.01$).

Within 14 months after irradiation (Fig. 1(B)], the nature of he accumulation of I^{131} in the irradiated dogs was approximately he same as in the preceding experiment. However, we should note hat in this experiment the general level for the accumulation of ^{131} in the thyroid gland was lower than in the previous series or the control animals as well as for the irradiated dogs. Obiously, the reason for such a difference is the fact that in the irst case the function of the thyroid gland was examined in ebruary and March, while in the second case it was examined in ugust. Here, too, the curve for the accumulation of I^{131} in one rradiated animal (No. 218) was characterized by a rapid decrease. ithin 24 hours after the administration of I^{131}, the number of ulses for the irradiated dogs was lower than for the control by 6% ($t = 2.68$; $0.1 > p > 0.05$). Although the dogs which contracted cute radiation sickness in some cases showed an increased percentage of organically-linked iodine in the blood plasma, these animals did not show symptoms which were typical of hyperthyreosis [3]. /394 This conforms with the clinical data [14].

The thyroid gland is a radiation-resistant organ [18]. Therefore, we scarcely have a basis for assuming that its dysfunction within several months after the general irradiation in a dose of 400 r can be explained by direct injury to the thyroid tissue. Obviously, a disorder in the function of the thyroid gland indicates changes in the regulation of its activity on the part of the hypothalamus, whose sensitivity to irradiation has been proven indisputably [12, 16].

Table 1 shows the results of determining the cholinesterase activity in the hypothalamus and thalamus of dogs within 14 months after irradiation. Considering the close functional relationship between the midbrain and other regions of the cerebrum, the cholinesterase activity was also examined in the preperiform-periamygdalar and frontal-limbic regions of the cortex and in the hippocampus. The cholinesterase activity in the hypothalamus was exam-

TABLE 1. ACCUMULATION OF I^{131} IN THE THYROID GLAND, AND CHOLINESTERASE (CE) ACTIVITY IN THE HYPOTHALAMUS AND THALAMUS, FOR DOGS WITH ACUTE RADIATION SICKNESS

Group of Animals	No. of Dogs	Accumulation of I^{131} with in 24 Hours After Administration, impulses/min	CE Activity, μmole/100mg Hypothalmus	Thalamus
Control	125	340	10,52	6,42
	766	220	6,63	6,55
	598	310	10,51	5,55
	713	175	5,24	9,47
	872	345	6,55	10,70
	904	130	8,01	6,63
	624	300	5,64	6,21
$M \pm m$		280±32 (282±20)	7,54±0,84 (7,50±0,99)	7,34±0,69 (7,47±0,87)
Irradiation	495	110	5,50	3,38
	9	430	4,67	5,18
	23	182	5,60	3,31
	22	200	5,45	4,87
	21	140	5,52	5,50
$M \pm m$	—	212±90 (158±20)	5,33±0,18 (5,52±0,02)	4,4±0,46 (4,2±0,54)
p	—	>0,05 (<0,01)	<0,001 (<0,001)	<0,001 (<0,001)

NOTE: The numbers in parentheses show the data which excludes 9 and 904 dogs.

ined in the anterior and posterior regions separately (Table 2). /395

As we can see from Tables 1 and 2, the cholinesterase activity in the hypothalamus and thalamus of the irradiated dogs was statistically reliably lower than in the control ($p < 0.001$). In the control dogs, the cholinesterase activity in the posterior hypothalamus was higher than in the anterior region. In the animals which contracted severe radiation sickness, the activity of this enzyme was lower than in the control, by 19% in the anterior region of the midbrain ($p < 0.05$), and by 47% in the posterior region ($p < 0.05$).

In the other regions of the brain which we studied, the differences in the cholinesterase activity between the control and irradiated dogs were statistically unreliable.

Thus, a decrease in the accumulation of I^{131} in the thyroid glands of the irradiated dogs is accompanied by a decrease of the cholinesterase activity in the hypothalamus and thalamus.
Averson Pearse [23] showed that a stimulation of the supraoptic and

TABLE 2. ACCUMULATION OF I^{131} IN THE THYROID GLAND AND CHOLINESTERASE (CE) ACTIVITY IN THE ANTERIOR AND POSTERIOR REGIONS OF THE HYPOTHALAMUS (AH AND PH), THALAMUS (T), PREPERIFORM-PERIAMYGDALAR REGION (PP), HIPPOCAMPUS (H), AND FRONTAL-LIMBIC (FL) REGION OF THE CEREBRAL CORTEX, AND THE CEREBELLUM (C) FOR DOGS, 14 MONTHS AFTER γ-IRRADIATION IN A DOSE OF 400 r.

Group	No. of Dogs	I^{131}, impulses/min	CE Activity, μmole/100mg						
			AH	PH	T	PP	H	FL	C
Control	490	190	8,52	11,33	7,43	1,64	3,90	2,34	9,87
	500	260	8,91	10,94	5,85	1,63	4,08	2,21	10,25
	494	222	8,85	15,81	5,60	1,66	3,67	2,12	5,16
$M \pm m$		224	8,73	12,66	6,28	1,64	3,88	2,22	8,43
		±20	±0,12	±1,57	±0,72	±0,01	±0,14	±0,08	
Irradiation	172	150	6,03	4,92	5,35	1,27	4,03	4,35	—
	198	168	7,75	7,73	5,10	3,61	3,82	2,41	4,12
	218	182	7,70	7,50	4,95	1,48	3,78	2,13	7,96
$M \pm m$		166	7,13	6,70	5,13	2,12	3,87	2,96	6,04
	—	±9	±0,56	±0,90	±0,14	±0,86	±0,09	±0,87	
p	—	>0,05 <0,1	<0,05	<0,05	<0,1	>0,5	>0,5	>0,5	

Note: The function of the Thyroid gland was determined the day before the animal was killed.

paraventricular nuclei by a prolonged administration of thiouracil /396 brings about a decrease in the general esterase activity in the supraoptic nuclei. Similar changes were also found in the nedial nuclei of the thalamus. On the other hand, Schreiber [26] showed that the administration of the cholinesterase inhibitor *DFP* into the hypothalamic region intensifies the hypertrophy of the thyroid gland caused by the goitrogenic substances.

It is interesting that, in the microscopic examination of the thyroid gland in the experimental dogs, we first noted extreme hypertrophy and hyperplasia of the epithelium, almost complete resorption of the colloid, and a decrease in the number of follicles (Fig. 2). It seemed of definite interest to examine any relationship between the function of the thyroid gland and the cholinesterase activity of certain regions in the brain by the correlation method. The correlation coefficient (ρ^s) was determined according to Spearman's formula.

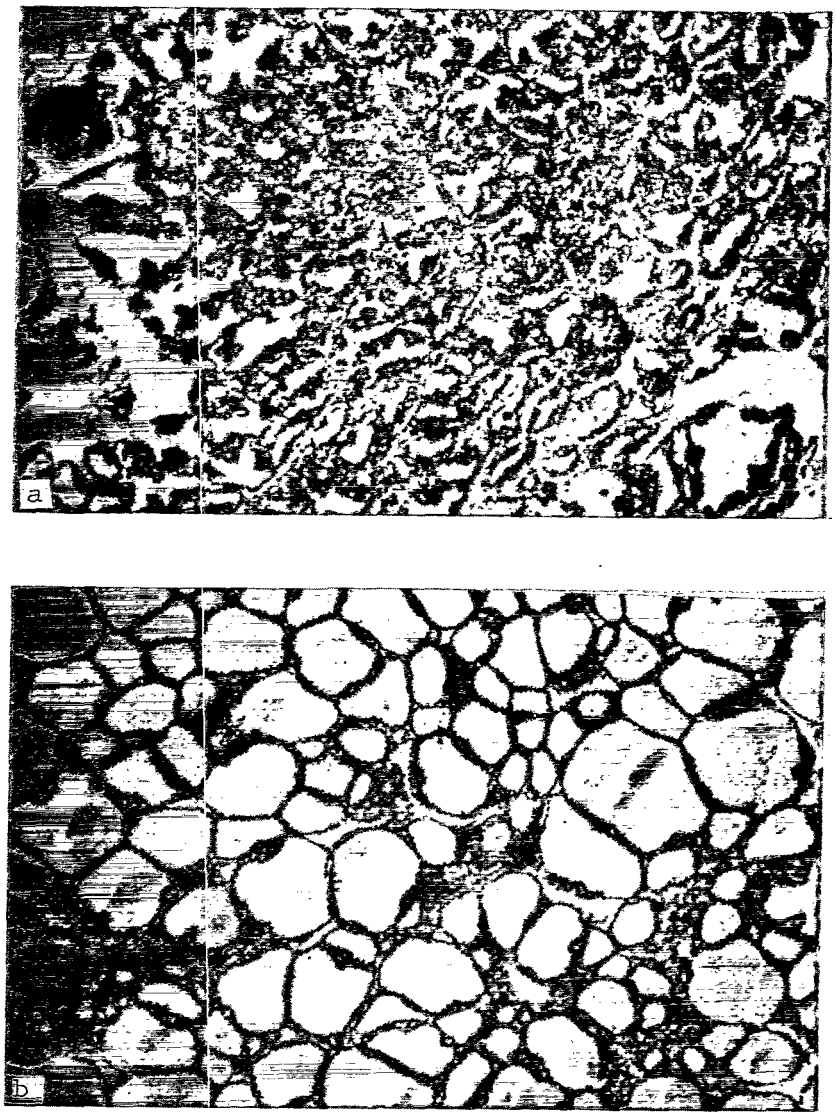

Fig. 2. Thyroid Gland of an Intact Dob (b), and 14 Months After Irradiation (a). Staining with Hematoxylin-Eosin, 75 x. /397

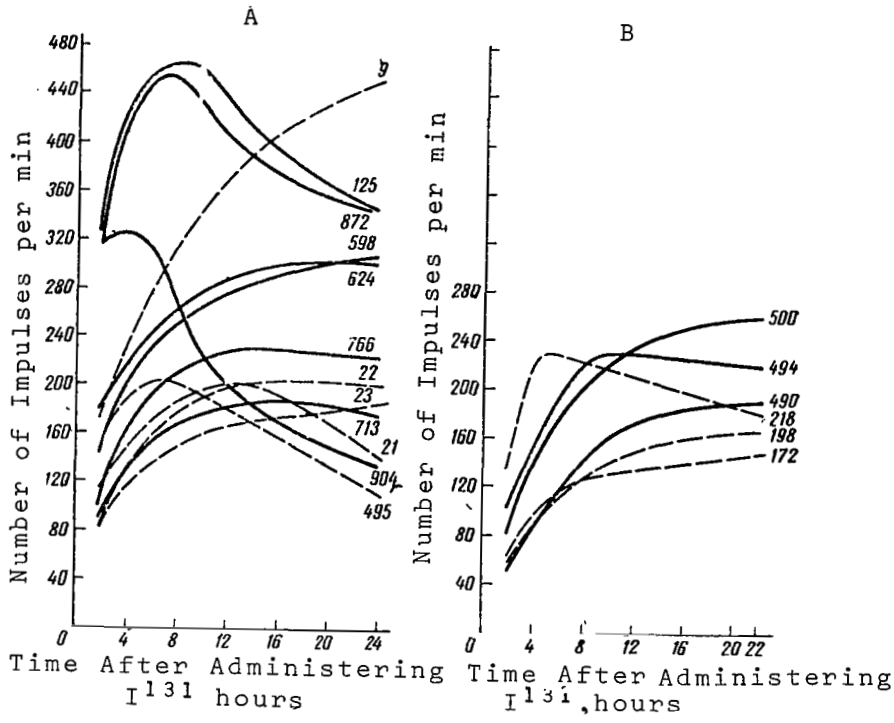

Fig. 1. Absorption of Radioactive Iodine by the Thyroid Gland in Dogs, 9 (A) and 14 (B) Months After General Irradiation in a Dose of 400 r. Dogs Nos. 9, 21-23, 172, 198, 218, and 495 were Irradiated; the Remaining Numbers are for Control Animals.

TABLE 3. CORRELATION BETWEEN THE ACCUMULATION OF I^{131} IN THE THYROID GLAND AND THE CHOLINESTERASE ACTIVITY IN THE HYPOTHALAMUS AND THALAMUS

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Group	No. of Animals	I^{131}-Hypothalamus	I^{131}-Thalamus
Control	7	+0,29 (+0,54)*	—0,1 (+0,02)
Experimental . .	5	—0,1 (+0,8)	+0,2 (0,0)
Control+Experimental	12	+0,18 (+0,77)	+0,25 (+0,59)

* The numbers in the parentheses show data excluding dogs. 904 and 9 (see Table 1).

Table 3 shows the ρ^s between the accumulation of I^{131} in the thyroid gland and the cholinesterase activity in the hypothalamus and thalamus for experimental and control dogs. The ρ^s between these indices was also determined in a combined selection (control + experiment). As we can see from Table 3, the ρ^s was small in the control and experimental groups. However, if the calculation for the ρ^s in the control group excludes Dog No. 904, and excludes Dog No. 9 in the experimental group, then the ρ^s between the accumulation of I^{131} and the cholinesterase activity in the hypothalamus increases up to +0.54 and +0.80, respectively.

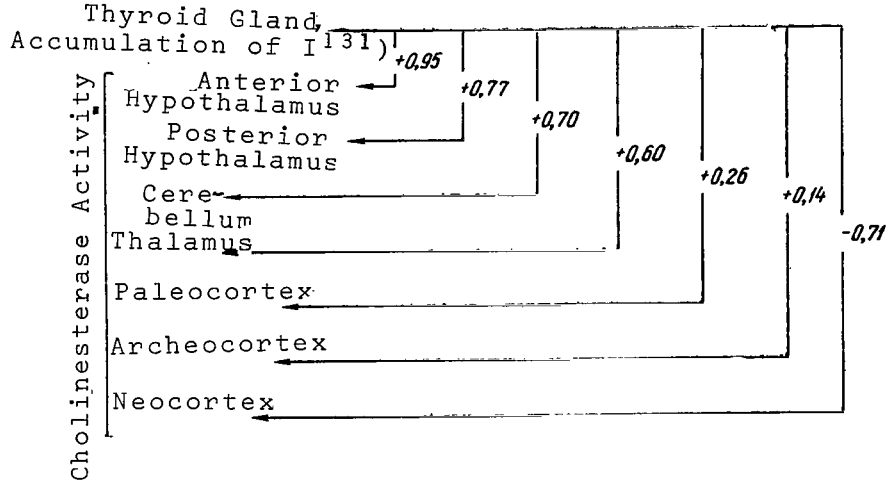

Fig. 3. Correlation Coefficient between the Accumulation of I^{131} and the Cholinesterase Activity in Certain Regions of the Brain.

Figure 3 shows the ρ^s between the accumulation of I^{131} in the thyroid gland and the cholinesterase activity in certain regions of the brain: the anterior and posterior regions of the hypothalamus, thalamus, cerebellum, preperiform-periamygdalar region of the paleocortex, hippocampus (archeocortex), and the frontal-limbic region of the neocortex. In the series of experiments, the function of the thyroid gland was examined one day before determining the cholinesterase activity. We should mention that in determining the ρ^s between the indices being examined, the experimental and control groups were combined. From the point of view of statistics, we did take liberties in this case in combining selections of different types. /399

In analyzing Figure 3, we should note the fact that the value for the correlation coefficient decreases from the anterior regions of the hypothalamus to the neocortex. The most pronounced positive relationship for the function of the thyroid gland is observed in the anterior region of the hypothalamus (ρ^s = +0.95), which conforms with certain physiological studies on the regulation of the tyrotropic function of the hypophysis, mainly by the nuclei of the anterior region of the midbrain [1,15,17]. Many so-called extrahypothalamic regions of the brain also have a definite regulatory

role in relation to the endocrine functions. However, these effects do not directly involve the nuclei of the hypothalamus [6]. There are data which show a direct relationship between the hypothalamic region and the cerebral cortex, particularly in the limbic and orbital regions of the hemisphere. The relationships to the limbic region probably occur within the limits of a definite functional sphere which includes the mammilary corpora, the anterior nucleus of the thalamus opticus, the limbic cortex, the hippocampus, the fornix, and the mammilary corpora again [19]. The correlation coefficients for the thyroid gland-cerebellum and the thyroid gland-posterior hypothalamus are very close in value: +0.70 and +0.77, respectively. It is interesting that the effect of the cerebellum on the vegetative functions of an organism occur (as the studies of L.A. Orbeli et al. showed [9,11], indirectly) through the effect on the hypothalamic and thalamic centers. Obviously, the correlation coefficients obtained for the accumulation of I^{131} and the cholinesterase activity could reflect (to some degree) the functional links between the thyroid gland and various regions of the cerebrum. It is certain that the correlation coefficients presented do not in any way reflect a cause-effect relationship. However, they can be used in analyzing the interrelated functions of the endocrine glands and different regions of the brain, both as a norm and for examining various extremal effects of space flight.

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RATE OF POST-RADIATIONAL RECOVERY, WITH PARTIAL SHIELDING OF ORGANS IN THE ABDOMINAL CAVITY

V.I. Davydov, V.S. Morozov, and B.L. Razgovorov

ABSTRACT: The period of half-recovery in mice and rats, with the upper part of the animal's body shielded, was determined by the method of repeated irradiation. The mass of shielded tissue was about 12% of the entire body mass, and the remanent dose beyond the shield was 3-5.5%.

The half-recovery period for the protected animals was approximately three times less than for the controls.

Studies involving an explanation of the rate of recovery processes following non-uniform irradiation of the body are of great interest in space radiobiology, since the contributions of individual systems and organs to compensation for radiation damage are unquestionably dissimilar. /400

A number of authors [1,4,7] have attempted to evaluate the rate of recovery after partial or non-uniform irradiation of animals. After non-uniform or partial irradiation of dogs (the head received a dose of 845 r, the trunk a dose of 175 r), the period of half-recovery lasted 8.6 days and was close to the same characteristic for a general uniform irradiation at a dose of 175 r (7 days); for a uniform irradiation at a dose of 300 r, it lasted 16.9 days [1]. For rats, with only the lower half of the body irradiated, the period of half-recovery lasted 1.7 days, while it lasted 7 days for irradiation of the upper half of the body [5]. /401

Obviously, we can state that, for each region or organ (or at least for the most radiation-sensitive regions of the body) there are various coefficients for the rate of recovery (β), the sum total of which (and possibly a more complex combination) also gives β for general irradiation. In a first approximation, we can consider that $\beta_1 > \beta_2$, where β_1 is the rate of recovery for the organs in the abdominal cavity (mainly the intestine), and β_2 is the rate of recovery for the hemopoietic system. We should mention, however, that this can be valid only for the method of repeated irradiation, for the reparative processes at the level of the tissues and the cells, and (to a lesser degree) for the regulatory functions of an organism.

The authors attempted to examine the effect of shielding organs (in particular, the organs in the abdominal cavity or separate sections of the body) on the rate of the recovery processes.

The experiments were conducted on 410 white mice (males) weighing 19-22 g, and on 600 rats of both sexes (50% male + 50% female) weighing 220-250 g. The animals were subjected to a general γ-irradiation in an experimental irradiator with a charge of Co^{60}, at a dose rate of 12 r/min.

For the first irradiation, we shielded the upper region of an animal (in half the animals) with the aid of metal plates with a width of 1 cm for the mice and 2 cm for the rats. The density of the shield in the first case was 90 g/cm, and 117 g/cm in the second case. For the rats, the mass of shielded tissue was about 12% of the entire mass of the body, while the remanent dose beyond the shield was about 3.5%. For the mice, these values were somewhat higher, 5.5%. The methods for shielding the organs in the abdominal cavity and for irradiating the animals have been described in greater detail in studies by B.L. Razgovorov, V.S. Morozov, et al., [2-3].

The control and protected mice were subjected to an initial irradiation with doses of 300,500,700, and 900 r; after 5 days, they were all irradiated again with a dose of 600 r. The control rats were irradiated first with a dose of 360 r, and the shielded rats with a dose of 840 r. All the rats were irradiated again with doses from 400 to 800 r, 2, 7, 14, and 21 days after the first irradiation.

In order to determine the effective dose, we plotted the calibration dose-effect curves for a general γ-irradiation of mice and rats at dose rates of 280 and 12 r/min, respectively. The calibration curves were expressed in the form of regression equations: /402

$$\log D = 2.380 + 0.097 \cdot P \text{ (for the rats), and}$$
$$\log D = 2.225 + 0.110 \cdot P \text{ (for the mice),}$$

where D is the irradiation dose, and P is the fatality rate, in deaths.

The fit of the death-lines to the experimental points was tested with the aid of the criterion χ^2. In both cases, the coincidence of the experimental data with the equations for the death-lines was statistically reliable ($p < 0.005$).

The results of the experiments conducted are shown in Tables 1 and 2. In analyzing the experimental materials and calculating the half-recovery periods ($T_{0.5}$) and the constants for the recovery (β), we used two models: an exponential model without an irreversible component ($f = 0.0$), and one with $f = 0.1$-0.2.

It follows from Table 1 that the value of β for the control mice is 0.182-0.099, while it is 0.530-0.405 for the mice which were shielded around the abdomen. We should note that the value for β depends on the dose in the first irradiation. Figure 1 shows

TABLE 1: VALUE FOR REMANENT RADIATION DAMAGE IN MICE, 5 DAYS AFTER γ-IRRADIATION, WITH AND WITHOUT SHIELDING OF THE ABDOMINAL REGION.

Group	First Dose, r (D^1)	Second Dose, r (D^2)	No. of Mice	Deaths by the 30th Day, %	D_e, r	$(D_e - D_e^2)$, r	$(D_e - D_e^2)/D^1$	$T_{0.5}$, days	β ($f = 0,0$)
Control	300	600	17	53,0	650	120	0,400	3,8	0,182
	500	600	16	81,3	780	250	0,500	5,0	0,138
	700	600	20	90,0	880	350	0,500	5,0	0,138
	900	600	20	100,0 (97,3)**	1030	500	0,555	7,0	0,099
Shielding* of the Abdominal Region	300 [120]	600	20	10,0	462	—68	—0,227	<1,3	>0,530
	500 [200]	600	20	30,0	560	30	0,060 [0,150]	1,3 [1,9]	0,530 [0,364]
	700 [280]	600	17	41,1	600	70	0,100 [0,250]	1,5 [2,5]	0,460 [0,276]
	900 [360]	600	20	50,0	645	115	0,128 [0,320]	1,7 [3,0]	0,405 [0,230]
	—	600	17	23,5	530 (D_e^2)	—	—	—	—

*Shielding during the first irradiation (D^1).

**The percentage of deaths for a dose of 900 r are given in parentheses. This was obtained according to the formula: $\log D^1 = 1.250 + 0.246 \cdot P$, where P is the mortality in deaths. The numbers in the brackets give the data obtained by calculating the coefficient of the decrease in the biological effect of the radiation for shielding the abdomen as equal to ~ 2.5 [3].

the data on the change in the degree of the remanent damage versus the first irradiation. It is interesting that within 5 days after irradiation with a dose of 300 r (shielding the abdominal region) $L_0 < 0$, i.e., the radiation-sensitivity of these animals to the repeated irradiation was lowered, while for the other groups, $L_0 > 0$. The dashes show the extrapolated part of Curve 1 (for the control animals). Curves 1 and 2 correlate with each other. The half-recovery period for the animals which were shielded in the abdominal region is approximately 3.8 times less than for the control mice. We can assume that this is linked with the decrease in the biological effect of the radiation by shielding the abdominal region. If we take the coefficient for the decrease in the biological effect of the radiation produced shielding this region, as equal to ~ 2.5 [3], then the corresponding calculations show that the rate of recovery under the shielded conditions is also approximately twice as high as for the control animals (Table 1). /403

TABLE 2: EFFECT OF SHIELDING THE ORGANS IN THE ABDOMINAL CAVITY ON THE RATE OF RECOVERY FROM RADIATION DAMAGE IN RATS.

Group	Interval between Irradiations, days	First Dose, r (D^1)	Second Dose, r (D^2)	No. of Rats	Deaths by the 30th Day, %	D_e, r	$(D_e - D^2)$, r	$(D_e - D^2)/D^1$	Average Value of L_0	β and $T_{0.5}$, days
Control	2	360	400	8	37,5	675	275	0,760	0,776	β ($f=0$) = 0,230, $T_{0,5}$ = 3,0; β′ ($f=0,2$) = 0,345, $T'_{0,5}$ = 2,0
			500	8	50,0	735	235	0,655		
			600	8	87,5	930	330	0,920		
	7	360	500	8	50,0	735	235	0,655	0,655	β ($f=0$) = 0,069, $T_{0,5}$ = 10,0; β′ ($f=0,2$) = 0,115, $T'_{0,5}$ = 6,0
			600	8	100,0	—	—	—		
			700	8	100,0	—	—	—		
	14	360	550	8	25,0	630	80	0,222	0,347	
			675	8	75,0	840	165	0,460		
			800	8	87,5	930	130	0,360		
	21	360	550	8	62,5	780	230	0,640	0,467	
			675	8	62,5	780	105	0,292		
			800	8	100,0	—	—	—		
Shielding the Abdominal Region	2	840	400	8	75,0	840	440	0,525	0,517	
			500	8	87,5	930	430	0,510		
			600	8	100,0	—	—	—		
	7	840	500	8	50,0	735	235	0,280	0,280	
			600	8	75,0	840	240	0,286		
			700	8	87,5	930	230	0,274		
	14	840	550	8	75,0	840	290	0,345	0,345	
			675	8	100,0	—	—	—		
			800	8	100,0	—	—	—		
	21	840	550	7	71,4	810	260	0,309	0,304	
			675	8	87,5	930	255	0,302		
			800	8	100,0	—	—	—		

* Shielding during the First irradiation.

Table 2 shows the calculations obtained in determining β with /404
f = 0.00 and f = 0.20[1], for rats with shielded abdomens and control

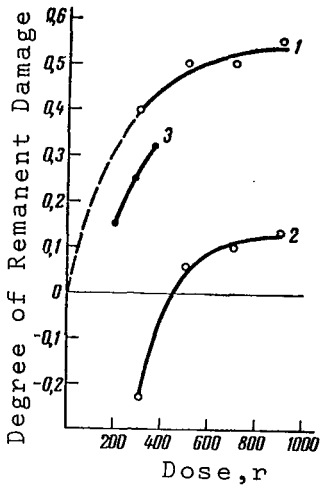

Fig. 1

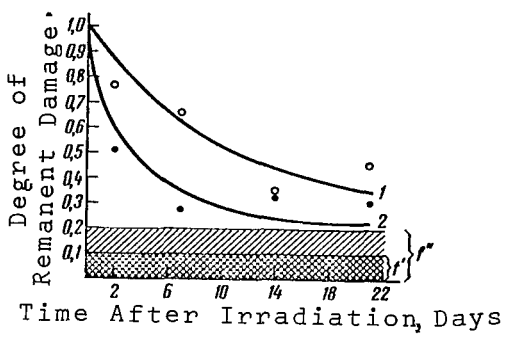

Fig. 2

Fig. 1. Value for the Remanent Radiation Damage in Mice Versus the Dose in the First Irradiation. (1) General Irradiation: (2) Irradiation with Shielding of the Abdominal Region; (3) Same as (2), but Considering the Weakening of the Biological Effect of the Radiation by Shielding the Abdomen. (On the left side-) Degree of Remanent Damage; (On the bottom-) Time After Irradiation, Days.

Fig. 2. Decrease in the Degree of Remanent Radiation Damage for General Irradiation (1) and Shielding the Abdominal Region (2); f' and f'' are the Values of the Irreversible Component, 10 and 20%, Respectively. (On the left side-) Degree of Remanent Damage; (On the bottom-) Time After Irradiation, Days.

rats; Figure 2 shows the relationship between the degree of remanent damage and the time after the first irradiation. The values obtained for $T_{0.5}$ are the following: 10 days for the control animals (f = 0.0), and 6 days (f = 0.2); for the rats with shielding of the organs of the abdominal cavity, 3 and 2 days, respectively. Thus, the $T_{0.5}$ for the rats which were shielded around the abdominal cavity, just as for the mice, is 3 times less than for the control animals.

Obviously, there are no contradictions between our data and /405
the results obtained by Blair, who showed that the rate of recovery after irradiating the abdominal cavity was higher than when it was shielded. The fact is that if we examine the recovery from the

[1]If the value f = 0.1 ± 0.1 (0.00-0.20), the error in determining the half-recovery period will not be greater than 17% [6].

radiation damage with shielding of the abdominal region, in this case the recovery rate determined will be lower than for irradiation of the abdominal region alone. In our experiments, the recovery rate was examined for heterogeneous irradiation, i.e., the first dose (with shielding) and the second dose (without it).

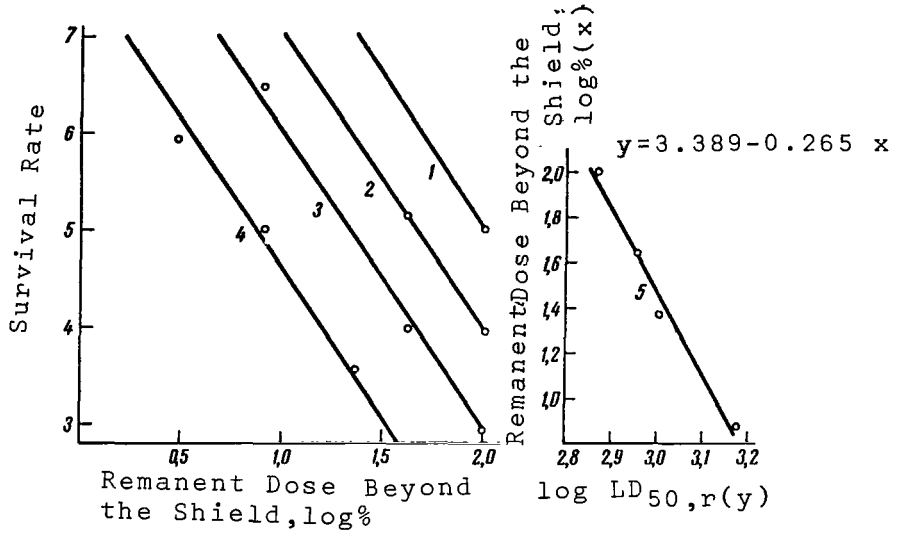

Fig. 3. Nomogram Showing the Relationship Between the Survival Rate, the Remanent Dose Beyond the Shield, and the Dose for Irradiating the Rats. (1) 740; (2) 900; (3) 1000; (4) 1500 r; (5) Line for Determing the Other Doses.

We can assume that, if $|D_e^k + D^2| = |D_d|$, then the accelerated recovery which was found is, in fact, invalid; if $|D_e^k + D^2| < |D_d|$, then an acceleration is actually not observed. $|D_e^k + D^2|$ and $|D_d|$ are the biological effects (for example, the percentage of deaths) of an irradiation repeated twice after the corresponding time interval, and a non-uniform single irradiation, respectively (in our case, the irradiation is non-uniform because the abdominal region is shielded); D_e^k is the effective dose for the shielded animals, determined by the assumption that the recovery rate is the same as for the controls, i.e., $\beta(f = 0.2) = 0.115$; D^2 is the second dose of irradiation; D_d is the dose with heterogenous or non-uniform irradiation, with a remanent dose $d(\%)$ of the irradiation beyond the shield.

In order to conduct the corresponding calculations shown in Table 3, we first determined the relationship between the survival rate for the animals and the value for the remanent dose beyond the shield and the dose of irradiation, on the basis of the experimental data (Fig. 3). As we can see from this nomogram, Lines 2, 3, and 4 are parallel to each other. Curve 1 of this figure was constructed on the basis of accepting a rectilinearity for all the

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corresponding lines, at least within the range of doses of 700-1500 r.

TABLE 3: COMPARISON OF THE BIOLOGICAL EFFECT FOR A TWICE-REPEATED IRRADIATION (D^1 WITH SHIELDING AND D^2 WITHOUT IT), AND FOR A SINGLE HETEROGENEOUS IRRADIATION (PARTIAL SHIELDING OF THE ORGANS IN THE ABDOMINAL CAVITY)

Twice-Repeated Irradiation						Single Irradiation			
D^1, r	D^2, r	Mortality, % (1)	$D_e^k + D^2$	$D_e^k + D^2$	$\frac{D^2}{D_e^k + D^2}$ (H_0), %	D_d	$d = H_0$, %	Mortality, % (2)	$\Delta_{(2)-(1)}$, %
840a	500	87,5	688	1188	37,8	1188	37,8	91,3	3,8
840a	400	75,0	688	1088	36,8	1088	36,8	78,8	3,8
840b	600	75,0	468	1068	56,0	1068	56,0	90,4	14,4
840b	500	50,0	468	968	51,5	968	51,5	61,8	11,8

Note: D^1 and D^2 are the same as in Table 1; D_e^k is the effective dose for a recovery rate $\beta(f = 0.2) = 0.115$; D_d is the dose for non-uniform irradiation with a remanent dose d (%) beyond the shield; a is the interval between D^1 and D^2 (2 days), and b is the same (7 days).

In order to obtain the line for the other doses which are not given in Figure 3, we can use line 5, or the formula which establishes a relationship between the remanent dose beyond the shield (shield-width of 2 cm) and $LD_{50/30}$:

$$\log (LD_{50/30}) = 3.389 - 0.265 \cdot \log d_{50}.$$

It follows from Table 3 that the mortality for a twice-repeated irradiation is lower than for a single non-uniform irradiation. Thus, the difference in mortality rates between the single and twice-repeated irradiations with an interval of 2 days was +3.8 (7 days, 11.8 to +14.4%).

In our experiments, in order to determine D_e^k, we used β for a general uniform irradiation, although, if we exclude the effect of the organs in the abdominal cavity on the recovery processes, β should be much less for the remaining organs of the body. Thus, if we conduct our calculations with $\beta < 0.115$, the difference found between the deaths of the animals for these variations of irradiation will be much greater. The deficit found for $\Delta_{(2)-(1)}$ Table 3) shows the presence of a more intensive postradiation recovery /407 after a partial shielding of the organs in the abdominal cavity than after a general irradiation. This deficit will be greater if we assume that $\beta < 0.115$ in our experiments, which is completely admissible.

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EXAMINING THE RBE OF PROTONS AND HEAVY IONS ON LYSOGENIC BACTERIA

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ABSTRACT: An examination was made of the relative biological effectiveness (RBE) of protons with energies of 630 and 100 MeV, and of accelerated carbon ions with energies of 36 MeV, on the lysogenic bacteria of the bacillus E. Coli (λ).

It was established that the RBE coefficients for the protons of these energies, in relation to γ-rays from Co^{60}, vary within the limits of 0.9-1.0 (according to the test of inducing phagoproduction and inactivation of the bacterial cells). The accelerated carbon ions have a more pronounced inducing effect. The RBE of the particles varied from 1.5 to 4.0, depending on the dose.

The appearance of an oxygen effect was shown, as was the lack of any significant effect of the dose rate (from 0.3 to 35 rad/sec) of the proton radiation on the radiation-sensitivity of the bacteria which produce induced bacteriophages.

At the present time, the determination of the doses which astronauts receive is being made solely on the basis of the indices from physical dosimetric devices (individual and on-board dosimeters). Despite the great accuracy of these devices, their indices characterize only the absorbed dose in physical rad-units, and they do not account for the values of the relative biological effectiveness (RBE) of the radiations, which can vary according to the spectral and qualitative characteristics of individual types of cosmic radiation. /407

In relation to the practical necessity for working out biological dosimetry under the conditions of space flight, we find it necessary to conduct model experiments, especially on those biological objects which have already been used repeatedly in experiments in space. An example of such biological dosimeters for space radiation, established by studies of French and Soviet researchers, is given by lysogenic bacteria, which have a very high sensitivity to the inducing effect of ionizing radiation [3,4,11-16]. /408

However, we should note that such a set-up for the problem can be valid only after conducting preliminary examinations with terrestrial experiments, in order to clarify the nature of the radiation effects obtained by using lysogenic bacteria and other

objects which are at a higher level of biological organization.

Despite the obvious advantages of the lysogenic system of bacteria (the high radiation-sensitivity, the strict additivity of the effect for prolonged radiation, the relative simplicity in handling and the possibility of conducting the experiments under the most varied conditions, etc), this model still is not being used sufficiently in radiobiological studies. We know of only a few studies involving a comparative examination of the biological effect of various types of ionizing radiations on this system [7,8,10].

Obviously, the use of lysogenic bacteria is also advantageous in clarifying the primary mechanisms for radiation damage and for protection from genetic anomalies [1, 2, 5, 6].

In this article, we examined the relative biological effect of protons with energies of 630-50 MeV, and of accelerated heavy carbon ions with an energy of 36 MeV, on the lysogenic bacteria E. coli K-12 (λ). We have also presented materials on the effect of the irradiation conditions and certain modifying factors on the radiation-sensitivity of lysogenic bacteria which were subjected to the action of protons. The evaluation of the effectiveness of these radiations was made on the basis of a comparison of the values for inducing intracellular development of a moderate phage (λ), during irradiation of a lysogenic culture of E. coli K-12 (λ) by protons, heavy carbon ions, and γ-rays of Co^{60}.

In all the experiments, we used a four-hour bouillon culture of the lysogenic strain of E. coli K-12 (λ) in a concentration of $2 \cdot 10^8$ microbial bodies per ml. The irradiation of the bacteria took place (depending on the problem and type of irradiation) in ampules, flasks, or petri dishes. In order to determine the quantity of bacteria which produced an induced phage, we used the direct method: the lysogenic culture was sifted out of the corresponding dilution immediately after irradiation, together with the indicator strain of E. coli C_{85} in an agar film. Since the value of the spontaneous background remains constant for the same experimental conditions, the degree of induced phagoproduction in relation to the radiation dose was easily determined by the ratio between the number of phage colonies counted in a growth area of the experimental samples and the number of spontaneous phage colonies in the control dishes. In the future, this ratio will be expressed by the symbol "*R*".

The survival rate of the bacteria was studied parallel to the /409
examination of the inducing effect.

As the source of radiation by protons and multiply-clarged carbon ions, we used the synchrocyclotron LYaP OIYaP and the cyclic heavy-ion accelerator U-150 LYaR OIYaP, respectively. The EGO-2 apparatus was used as the source of the γ-rays from Co^{60}.

The dosimetry of the protons was performed with the aid of ionizing chambers, individual luminescent dosimeters, and thermoluminescent glass plates placed with the samples.

The dosimetry of the heavy ions was conducted on the basis of the readings on a transistorized monitor, which was placed in a symmetrical position in relation to the samples.

The results of examining the inducing effect of the protons of 630 and 100 MeV and of the γ-rays of Co^{60} on the phagoproduction in the bacillus E. coli K-12 (λ) are shown in the table. In evaluating the results, we noted both the absolute number of bacteria which produced an induced phage and the ratio of the average values for induced phagoproduction in the experiment and in the control.

TABLE: INDUCTION OF PHAGOPRODUCTION IN A LYSOGENIC CULTURE OF E. COLI K-12 (λ) IRRADIATED BY γ-RAYS, PROTONS WITH ENERGIES OF 630-100 MeV, AND ACCELERATED CARBON IONS WITH AN ENERGY OF 36 MeV.

Dose, rad	Ratio between the no. of phage colonies in the experiment and the value for the spontaneous background in the Control (R)			
	γ-rays from Co^{60}	Protons, 630 MeV	Protons, 100 MeV	Carbon Ions
Control	1,0	1,0	1,0	1,0
50	3,1±0,33	—	2,51±0,50	3,9± 2,2
100	5,3±0,52	4,10±0,39	4,64±0,53	6,5± 1,4
200	6,9±0,78	6,80±0,56	6,11±0,69	24,0± 2,8
400	13,0±0,83	11,0 ±0,91	11,5 ±1,24	55,0± 6,8
800	20,1±0,16	17,0 ±1,44	18,1 ±1,95	67,0±10,7

The degree of phago-production induced during the effect of protons with 630 and 100 MeV and heavy carbon ions with 36 MeV is found to be clearly dependent on the dose (Fig. 1). This relationship has a graded character for all the energies of the proton radiations and γ-rays being examined, within a range from 50 to 800 rad. The relationship can be described by the following equation:

$$R = a \cdot D^b,$$

where R is the index for induction of a bacteriophage.

The curves of the relationship between the dose and the induction of phagoproduction for the protons of 630 and 100 MeV are in close proximity to one another. There was no statistically reliable difference noted between them.

Thus, there is no essential difference noted between the biological effect of protons of 630-100 MeV and that of γ-rays from Co^{60}. However, there is an insignificant but statistically reliable increase in the degree of phage induction under the influence of /410

γ-rays, in comparison with the protons of 630-100 MeV. This allows us to consider that the RBE of the protons of 630-100 MeV is equal to 0.9. The lack of reliable differences in the effects between the protons of 50 MeV and γ-rays shows that the RBE of the protons with these energies is equal to one unit.

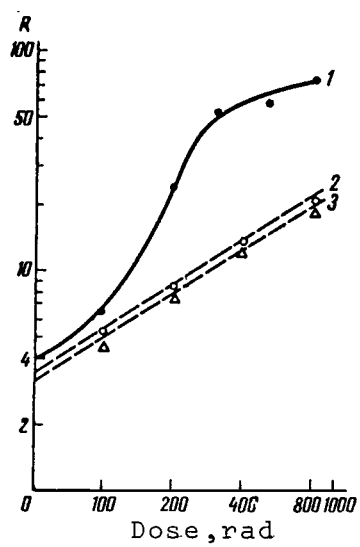

Fig. 1. Phagoproduction Induced by γ-Rays from Co^{60} (2), by Protons with an Energy of 630 MeV (3), and Accelerated Carbon Ions with an Energy of 36 MeV (1) Versus the Effective Dose.

Noteworthy results were obtained in examining the inducing properties of the heavy multiply-charged ions. As we can see from Figure 1, these particles have a much more pronounced inducing effect on phagoproduction than the standard types of radiation and protons. Of particular note is the clearly non-uniform character of the increase in the induction of phagoproduction versus the dose, as a result of which the corresponding dose-effect curve acquires an S-shape.

Interesting results were obtained in examining the effects obtained in the case of changes in the irradiating conditions and the effect of certain modifying factors. The complete identity in the character and intensity of the processes for radiational phage induction during the effect of protons of 630 MeV and γ-rays, despite the significant differences in the dose rate (0.3-35 rad/sec), allows us to draw the conclusion that there is no relationship between the magnitude of the effect observed and the dose rate.

In this study, we also attempted to examine the effect of partial oxygen pressure on phagoproduction. For this purpose, we examined the differences in the effective-dose relationship of the value for induction of phagoproduction with irradiation of the bacteria by protons (replacing all the oxygen with nitrogen) and at the normal partial pressure of oxygen (in air). The results of the experiments showed that the lysogenic bacteria we used react to the changes in the oxygen concentration in the same way as did other, previously-examined test-objects. The protective effect of anoxia on the induction of phagoproduction was clearly shown. The coefficients of oxygen intensification for the protons of 630 and 50 MeV were the same, within the limits of 2.4-2.6. The value for the coefficients remained generally constant throughout the entire range of doses from 50 to 800 rad. /411

In examining the effect of phagoproduction, we naturally also studied the survival rate of the bacteria and the change in their

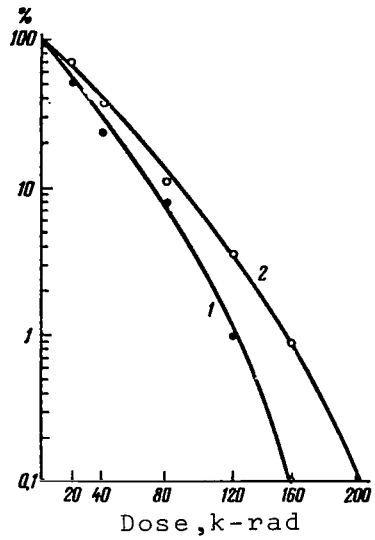

Fig. 2

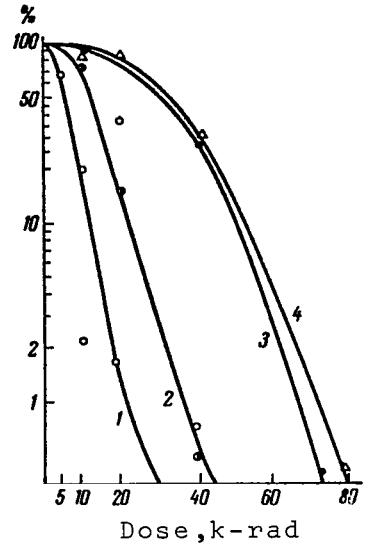

Fig. 3

Fig.2. Relationship between the Lethal Effect in the Lysogenic Bacteria E. coli K-12 (λ) and the Effective Dose of γ-Rays (1) and Protons of 630 MeV (2).

Fig. 3. The Effect of the Amount of Oxygen and Temperature on the Survival Rate for the Lysogenic Bacteria E. coli K-12 (λ). (1) Irradiation in Air at 0°; (2) Same, in Nitrogen at 0°; (3) Same, in Air at 37°; (4) Same, in Nitrogen at 37°.

radiation-sensitivity during the action of modigying factors. An analysis of the results showed that the principal quantitative characteristics for the injurious effect of the protons of 630 MeV on the bacteria E. coli K-12 (λ) remained the same when we examined their survival rate as when we determined the phagoproduction (Fig. 2). It was found, in particular, that the RBE of protons of 630 MeV (in relation to the γ-rays from Co^{60}) was equal to 0.9, in a comparison of the LD_{37} and the LD_{50}. Similar results were obtained in examining the oxygen effect (Fig. 3). The unexplained fact that the value for the oxygen effect and the injurious effect of the radiations clearly decreased during the irradiation of the bacteria under thermostatic conditions at 37°, in comparison with the irra- /412
diation at a temperature of the medium equal to 0°, was rather unexpected.

Therefore, the correlation observed in the RBE values for the radiation, obtained for the lysogenic system and other biological systems, shows that it is possible to use this system for studying the biological effectiveness of ionizing radiation with a varying density of ionization. The good agreement between the RBE values obtained for the heavy ions and the data in the literature [9,10]

and calculated data show the sufficient sensitivity of the experimental model to a change in linear losses of energy. This, in turn, can serve as an additional foundation for a more effective use of lysogenic bacteria as biological dosimeters in space experiments.

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THE DOSE-DEPENDENCE AND DYNAMICS OF THE PHYSIOLOGICAL REGENERATION OF THE EPITHELIUM IN THE CORNEAS OF MICE WHICH WERE SUBJECTED TO IRRADIATION BY PROTONS WITH AN ENERGY OF 630 MeV AND BY γ-RADIATION FROM Co^{60}

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ABSTRACT: A comparison of the rate of recovery of mitotic activity, the level of chromosome aberrations in the first mitosis, and the quantity of epithelial cells in the corneas of mice which were subjected to irradiation by γ-rays from Co^{60} and protons with an energy of 630 MeV showed that the values for the relative biological effectiveness (RBE), calculated on the basis of various criteria, differ substantially from one another, when using the rate of recovery of the mitotic activity as the criterion, the RBE value is equal to 1.1. At the same time, the RBE value calculated according to the maximum level for chromosome aberrations in the first mitosis is equal to 0.7. This value is close to the RBE values found during an analysis of the curves for the fatality rate. Multiple quantitative evaluations of the RBE made on the basis of studies of the changes in the number of epithelial cells in the corneas of irradiated animals give a value which is close to 1.

It is well known that the tissues of an organism are in a /413
state of dynamic equilibrium: the cells which die because of age are replaced (in the process of physiological regeneration) by young ones which come from a proliferative pool. The effect of high-energy protons entering into the composition of primary cosmic radiation on human beings and animals causes a suppression of the mitotic activity in the tissues, the appearance of pathological mitosis, and cellular destruction, which can then damage the entire tissue and its physiological activity. Moreover, damage to the hereditary structures of cells can cause the development of pathological processes at periods long after irradiation.

The above-mentioned phenomena were studied, using the model of the epithelium in the corneas of mice which were subjected to irradiation by protons at an energy of 630 MeV. In addition to methodological advantages, this model was selected because of the important role of the corneal epithelium in the process of visual perception, the very high requirements for entirety of the tissue and optical transparency of its cells, and the limited possibilities

for shielding the eye from radiation, linked with the necessity of using transparent material for these purposes. For a standard in determining the specific features of the biological effect of high-energy protons and their relative biological effectiveness (RBE), we used γ-radiation from Co^{60}.

METHODS

The experiments were conducted on mice of the CC57br strain, weighing 18-20 g. These animals were irradiated by protons with an energy of 630 MeV in doses of 100, 200, 700, and 1100 rad (dose rate of 31.9 rad/sec) on the sychrocyclotron of the Joint Institute of Nuclear Research at Dubna, and with γ-radiation from Co^{60} in doses of 200 and 700 rad (dose rate of 2.8 rad/sec) on the EGO-2 apparatus. The experimental animals were decapitated simultaneously with the controls at various times after irradiation. Since it is well known that the epithelium of the cornea in mice exhibits daily rhythms of mitotic activity whose amplitude can change because of irradiation [1,4], the animals were always decapitated at noon, /414 when the value of the mitotic index is equal to its average value per day [10]. During each period, we decapitated 6-15 experimental and 3-5 control animals; we used 320 mice in all in the experiments. The materials were fixed in Bowen's solution, and total preparations of the cornea were prepared. They were stained according to Karachi. In the preparations thus prepared, we could observe 3-4 layers of cells. However, only the two lower layers consisted of the homogeneous epithelial cells which have mitotic activity. The remaining one or two layers consisted of keratotic cells which, obviously were terminating their life cycle.

The number of cells within the field of vision of the microscope and the frequency of mitoses were measured by shifting the focus from the center of the preparation to the periphery; as a result, in order to determine the average values, we made calculations in the two lower reproductive layers of the cells at the periphery and the center of the cornea for the number of cells within the field of vision of the MBI-11 microscope with a magnification of 7 × 1.6 × 90, the number of mitoses per 1000 cells, and the relative percentage of chromosome aberrations at the stage of the anaphase (bridges and chromosome fragmentations).

RESULTS

It is natural to begin a study of radiation damage in the epithelium of the cornea with an analysis of the results of the "standard effect", irradiation by γ-rays from Co^{60}. The dose-dependance and the dynamics for the mitotic activity and the chromosome aberrations observed in this case, as well as the number of cells within the field of vision of the microscope, are given in Table 1.

It is well known that for tissues which are in a state of

equilibrium, the average value for the mitotic index is equal to the ratio between the average duration of the mitosis and the average life of the cell T, which in this case is equal to the average duration of the cell's stay in the two lower layers of the epithelium in the cornea. From this, we can determine T if the mitotic index and the average duration of the mitosis are known. If the mitotic index for the epithelium of the cornea is equal to $(9.09 \pm 0.53) \cdot 10^{-3}$, and the average duration for mitosis is 21 min [11], the value T is equal to 1.6 ± 0.1 days. Thus, out of the 178 ± 2 cells in the epithelium of the cornea in the control animals (within the field of vision of the microscope), 111 ± 7 cells will die within one day, and the same quantity of cells will again be formed in the process of cell division.

According to the data in the literature [16,19], the mitotic activity of cells is very sensitive to ionizing radiation, and is almost completely suppressed by radiation in doses on the order of several tens of rads. However, this process is reversible. It follows from this that irradiation in the dose range being examined causes practically complete suppression of mitotic activity, with subsequent recovery. From the data shown in Table 1, it is easy to establish that the rate of recovery decreases with an increase /415

TABLE 1. DOSE-DEPENDENCE AND DYNAMICS OF MITOTIC ACTIVITY, CHROMOSOME ABERRATIONS, AND THE NUMBER OF EPITHELIAL CELLS IN THE CORNEA, FOR THE EFFECT OF γ-RADIATION FROM Co^{60}

Dose, rad	Time between Irradiation and Decapitation, days	Mitotic Index (%)	Relative percentage of Chromosome Aberrations	No. of cells within the field of vision of the microscope
Control		9,09±0,53	0	178±2
200	1	5,28±0,49	0,447±0,044	168±2
	3	9,85±0,79	0,250±0,019	161±3
	5	8,61±0,77	0,139±0,021	170±1
	7	9,13±0,45	0,039±0,009	178±2
	10	8,07±0,26	0,012±0,005	179±1
700	1	1,77±0,11	0,695±0,057	177±4
	3	3,23±0,25	0,863±0,015	177±2
	5	5,45±0,34	0,647±0,019	159±2
	7	8,67±0,31	0,156±0,016	170±2
	10	8,54±0,45	0,057±0,019	174±3

of the dose. Actually, within one day after irradiation at a dose of 200 rad, the mitotic activity of the epithelium in the corneas of irradiated animals reaches roughly half of its original value, and is normal within 3 days after irradiation. In the case of irradiation at a dose of 700 rad, the 50%-level of mitotic

activity is achieved roughly within 5 days after irradiation, while normalization appears only on the 7th day. For a more rigid analysis of the results of studying the mitotic activity, we can attempt to approximate the curves for the recovery of the exponent and use its index as a quantitative criterion for the rate of recovery [10]. It was found to be equal to 0.86 per day in the case of irradiation in a dose of 200 rad, and 0.16 per day (i.e., 5.4 times less) in the case of irradiation in a dose of 700 rad.

In addition to the reversible inhibition of the mitotic activity, radiation can also cause changes in the genetic structure of a cell. The greatest change of this kind is seen in the chromosome aberrations. We attempted to evaluate the after effects of these disorders in a cell on the basis of an analysis of the changes in the relative number of chromosome aberrations in relation to time (Table 1). The relative percentage of chromosome aberrations for irradiation in a dose of 700 rad remains approximately constant during the first 5 days after irradiation, after which it rapidly decreases, reaching 22% of its original value by the 7th day and 8% by the 10th day.

It was shown earlier that, for a mitotic index of $(9.09 \pm 0.53)\cdot 10^{-3}$, the average duration for a cellular cycle is equal to 1.6 ± 0.1 days. The radiation effect causes a decrease of the mitotic index and a corresponding increase of the duration for the cellular cycle. The average value for the mitotic index for the first 5 days after irradiation is equal to $2.9\cdot 10^{-3}$, which corresponds to a duration for the cellular cycle of roughly 5 days. Thus, the cells show their first mitosis after irradiation during this period, while the changes in the relative number of chromosome aberrations reflect the differences in radiation sensitivity for the following stages of the mitotic cycle. We can see from the data in Table 1 that 0.695 of the cells which were at later stages of the mitotic cycle (and, therefore, the first to enter into mitosis) have damages of the genetic structures. Out of all the cells which were at the middle of the mitotic cycle during irradiation, 0.863 were damaged, while 0.647 of the cells which were at the beginning of the mitotic cycle were damaged. Therefore, we did not succeed in finding any sharp change in the radiation-sensitivity of the genetic structures in relation to the stage of the cell's mitotic cycle. The relative percentage of cells with genetic disorders, averaged according to the mitotic cycle, was equal to 0.735. /416

What is the subsequent fate of cells with genetic disorders?

One of us showed [9] that an irradiation of the cells in the epithelium of the cornea in doses which do not exceed 1000 rad has practically no effect on the mitotic apparatus: an incipient aberrant mitosis occurs at a normal rate and ends with formation of two daughter cells. However, as a result of the loss of genetic structures (related to fragmentation) or non-uniform distribution of the genetic material, with the presence of bridges formed as a

result of aberrant mitosis, the daughter cells lose their ability for unlimited reproduction, and form only limited colonies when cultured [14, 17, 18, 22-24]. The number of divisions of the damaged cell up to the moment of its reproductive destruction diminishes with an increase in the dose of irradiation.

Let us now examine the reproductive destruction (death) of the cells in the epithelium of the corneas of mice which were subjected to irradiation in a dose of 700 rad. As was already mentioned, the first mitotic cycle after irradiation lasts about 5 days. Similarly, we can show that the second mitotic cycle lasts from the 5th to the 7th day after the irradiation, and the third and fourth from the 7th to the 10th days. From the data shown in Table 1, we can easily see that during the second aberrant mitosis after irradiation, there were only 21.2% of the original number of injured cells which went through a first aberrant mitosis after irradiation (0.156 out of 0.735), and there were only 7.8% for the fourth aberrant mitosis (0.057 out of 0.735). The average number of divisions of an injured cell up to the moment of its reproductive destruction /417 is equal to 1.79.

Therefore, in the case being examined, the disorders of the genetic balance of a cell in the process of a first aberrant mitosis after irradiation cause the reproductive destruction of the cell in the following generation.

In a similar way, we can analyze the dynamics of chromosome aberration in the epithelial cells of the cornea in mice which were subjected to irradiation by a dose of 200 rad. In this case, the first mitotic cycle after irradiation ends during the period between the 2nd and 3rd days, while the original percentage of cells with genetic disorders covers a range from 0.447 to 0.250. During the following period, the mitotic index (and, thus, the duration of the mitotic cycle of the epithelial cells in the cornea) is practically the same as the norm. If we assume that the first cellular cycle ends around the 3rd day after the irradiation, while the average level of injury is equal to $(0.447 + 0.250)/2 = 0.349$, then the average number of cellular divisions up to the moment of reproductive destruction is equal to 2.31. We can see from the above that the average number of divisions of the aberrant cells prior to reproductive destruction diminishes with an increase of the dose, i.e., the degree of injury to the genetic structures of the cell increases. In addition, the number of injured cells also increases. The dose-dependence of the genetic effect of γ-radiation from Co^{60}, characterized by the maximum relative percentage of aberrant mitoses in the epithelium of the cornea in the irradiated mice, was exponential in the dose range being examined. The average effective dose was equal to 350 rad.

Finally, let us examine the results of measuring the number of cells within the field of vision of the microscope.

Among a number of factors which can cause a decrease in this index, we should mention the decrease in the appearance of new cells as a result of the suppression of the mitotic activity, and the increase in the appearance of dying cells, as a result of a disorder in the genetic balance during aberrant mitosis. We also have not excluded the possibility of injury to certain vitally-important structures of the cell and the so-called "interphasal destruction". However, we can easily see from the data shown in Table 1 that even for irradiation at the minimum absolute fatal dose of 700 rad for the mice, when the mitotic activity of the cells is deeply suppressed and about three-fourths of the cells have damage in the genetic structure, the change in the number of cells within the field of vision of the microscope is small. The maximum such change is reached around the 5th day after irradiation, when the number of cells within the field of vision decreases roughly by 10%, in comparison with the norm. At the same time, a single suppression of the mitotic activity during the first days after the irradiation, /418 when only 11 new cells appear in the field of vision (against 111 cells in the norm) in the case of preserving the normal intensity of 111 cells dying off per day within the field of vision should result in a cellular deficit of 111-11 = 100 cells in the vield of vision even in the first days after the irradiation, ot 56% of the normal value. Obviously, along with the suppression of the cell reproduction, the action of the cells tearing away from the tissue is also suppressed. A similar situation is also observed with irradiation of the animals by a dose of 200 rad.

An explanation for this fact, presented in great detail in other studies [3,10], is that the principal cause for the cells tearing away from the epithelium of the cornea in normal mice is the displacement of old cells by ones newly formed in the process of cellular division, so that the average lifespan for the cells of the tissue *T* is much shorter than their potential lifespan during the absence of cellular displacement. It follows that each destructive process whose intensity is less than the difference between the intensities for displacement and the natural dying-off of the cells will be compensated by a corresponding decrease in the displacement of cells. This circumstance does not allow for a detealled study of the destructive processes occurring in the epithelium of the cornea in the irradiated animals. We should only note that the maximum for the decrease in the number of cells roughly coincided in time with the maximum for the production of the mitotic index at a relative percentage of chromosome aberrations, i.e., the absolute number of pathological mitoses in the tissue. Such a coincidence indicates that the conclusion that aberrant mitosis leads to reproductive destruction and destruction of the cells is very probable.

Let us now turn to an analysis of the radiation injury of the epithelium in the cornea of mice which were subjected to irradiation by protons with an energy of 630 MeV (Table 2).

The average mitotic index of the epithelium of the cornea in the control animals was equal to $(9.78 \pm 0.62) \cdot 10^{-3}$, which corresponds to the average duration for a cellular cycle of $T = 1.5 \pm 0.1$ days. For each thousand mitoses, we found 5 aberrant ones on the average. The number of cells within the field of vision of the microscope coincided for all the control animals of both series.

In the case of irradiating the animals with a dose of 100 rad, recovery of the mitotic activity occurred during the first 1.5 days after the radiation effect. During the following 19 days, the mitotic index for the epithelium in the cornea of the irradiated mice was the same as the norm. When the animals received 200 rad, the mitotic activity was recovered around the 3rd day. However, during the period between 5.5 and 9.5 days after the effect, there was a repeated decrease of the mitotic index which was preserved up to the end of the study. With an increase in the dose of the irradiation up to 700 rad, the rate of recovery of the mitotic activity continued to decrease. However, we unfortunately did not succeed in tracing the dynamics up to the end. The mitotic index for the epithelium in the cornea of mice which underwent irradiation by a dose of 1100 rad did not reach 10% of its original value by the first day after the effect; then dropped almost to zero. /419

TABLE 2. DOSE-DEPENDENCE AND DYNAMICS OF MITOTIC ACTIVITY, CHROMOSOME ABERRATIONS, AND THE NUMBER OF EPITHELIAL CELLS IN THE CORNEA, WITH IRRADIATION BY PROTONS OF 630 MeV.

Dose, rad	Time between Irradiation and Decapitation, days	Mitotic Index (%)	Relative Percentage of Chromosome Aberrations	No. of cells within the field of vision of the Microscope
Control		9,78±0,62	0,005±0,003	178±2
	1,5	10,35±0,77	0,113±0,033	179±3
	2,5	8,60±0,55	0,092±0,021	168±2
100	5,5	9,82±0,68	0,050±0,015	183±2
	9,5	9,11±0,38	0,006±0,003	173±2
	20,5	9,15±0,50	0,003±0,003	173±1
	1,5	6,41±0,49	0,286±0,061	168±2
	3	9,55±0,47	0,160±0,023	166±4
200	5,5	9,60±1,08	0,066±0,019	170±2
	9,5	5,11±0,69	0,018±0,013	167±1
	20,5	6,41±0,68	—	174±1
	1,5	1,92±0,27	0,741±0,088	157±3
700	3	4,20±0,67	0,746±0,089	153±1
	6	4,87±0,60	0,316±0,036	146±6
	1	0,81±0,10	0,815±0,095	158±2
1100	3	0,09±0,03	0,857±0,101	134±3

Before evaluating the rate of recovery of mitotic activity, we must note that the curves which rise and fall repeatedly cannot be approximated for the entire path of one exponent.

As a result of this, we determined the exponential index characterizing the intensity of the recovery only for the beginning segment of the recovery curve, up to the first repeated decrease. It was equal to 0.71 per day, for irradiation in a dose of 700 rad. For the curves which corresponded to irradiation in doses of 100 and 1100 rad, we could not determine that index with any tenable degree of reliability.

Having compared the numerical values for the intensities of /420
recovering the mitotic activity of the epithelium in the cornea after the effect of γ-radiation from Co^{60} and high-energy protons in identical doses, we can determine the relative biological effectiveness (RBE) of the protons with an energy of 630 MeV by their capacity to suppress the restoration process. If we take as a measure of the radiation effect, the average effective recovery time, which is equal to the reciprocal of the rate of recovery and, in the mathematical sense, analogous to the average effective dose, the RBE of the protons with an energy of 630 MeV is equal to (0.86/0.71) = 1.21, for the case of irradiation at a dose of 700 rad, and (0.16/0.15) = 1.07, for the case of irradiation at a dose of 200 rad. The average RBE value for the dose range from 200 to 700 rad is equal to 1.14, i.e., the high-energy protons suppress cell reproduction more effectively than does the γ-radiation from Co^{60}. The RBE value evaluated on the basis of the remote effects is even higher, since the above-mentioned evaluations do not take into account the presence of a repeated drop in the mitotic activity in the case of proton irradiation being absent during irradiation by γ-rays from Co^{60}.

Let us now turn to a further study of the effect of the proton radiation on the genetic structures of the cells. From the data shown in Table 2, we can easily establish that the dose-dependence for the genetic effect of the radiation, characterized by the maximum relative percentage of aberrant mitoses in the epithelium of the cornea in the irradiated mice, is exponential within the limits of error in the experiment, within the dose range being examined. The average effective dose is equal to 540 rad. The RBE value of the protons with an energy of 630 MeV calculated according to the genetic effect was thus equal to (350/540) = 0.65.

In order to determine the degree of damage to the genetic structures of the cells, let us use the results of studying the dynamics for the relative percentage of aberrant mitoses. From the data shown in Table 2, we can easily establish that the average value of the mitotic index for the first three days after irradiation in a dose of 1100 rad is equal to $0.44 \cdot 10^{-3}$, while the corresponding value for the average duration of the mitotic cycle is 33.3 days. The average value of the mitotic index for the first

six days after irradiation by a dose of 700 rad is equal to $3.27 \cdot 10^{-3}$, while the corresponding value for the average duration of the mitotic cycle is 4.5 days. Thus, during this time after irradiation by a dose of 1100 rad, the cells enter only into a first aberrant mitosis, while, in the case of irradiation in a dose of 700 rad, the cells enter into a first and (partially) second aberrant mitosis. The relative radiation-sensitivity for the various stages of the mitotic cycle to the high-energy protons, as we can easily see from the data shown in Table 2, was similar to /421
the relative radiation-sensitivity to γ-rays. Since the after effects for a non-uniform distribution of the genetic materials in the process of aberrant mitosis can be found only in the daughter cells, we could not determine the number of divisions after the irradiation in doses of 700 and 1100 rad (and therfore the number of aberrant cells formed until reproductive destruction) because of insufficient time for observation. However, the time we had was long enough to determine this value in the case of irradiation in doses of 100 and 200 rad. The average number of divisions in the aberrant cells until reproductive destruction was equal to 3.01 for irradiation in a dose of 100 rad, and 2.34 for irradiation in a dose of 200 rad.

As was the case for irradiation by γ-rays from Co^{60}, the degree of damage to the genetic structures of a cell increased with an increase of the dose, and the average number of divisions in the aberrant cells until reproductive destruction, decreased.

Interesting information can be obtained by analyzing the dynamics and dose-dependence of the changes in the number of epithelial cells in the cornea of mice which were subjected to the effect of protons with an energy of 630 MeV. Irradiation in a dose of 100 rad causes a decrease in the number of cells within the field of vision approximately by 5%. A decrease of this index, which is close in value to the other, can be observed in the case of irradiation in a dose of 200 rad, as can easily be established from the data in Table 2. It is possible that in the latter case the recovery processes were suppressed because of the repeated decrease of the mitotic activity, so that the number of cells within the field of vision of the microscope remains decreased almost throughout the entire examination.

During a further increase in the irradiation dose, the amplitude of the decrease in the number of cells increases sharply, and, by the end of the experiment, reaches the following; 18% for irradiation of 700 rad, 25% for irradiation in a dose of 1100 rad. We should note that the decrease begins immediately after the irradiation, when the absolute number of pathological mitoses is small, because of the considerable suppression of the mitotic activity during this period. Thus, the destruction of the cells related to aberrant mitosis cannot be at all substantial in this case, and the so-called "interphasal destruction" is the principal contributor to the decrease in the number of cells.

Having compared the results of measuring the number of cells in the epithelium of the cornea for the mice which underwent the effect of γ-radiation from Co^{60} and protons with an energy of 630 MeV in various doses, it is easy to establish that the proton radiation , generally speaking, has a definite, specific injurious effect. The reason for this most probably is that the rate of the "interphasal destruction" of the cells which are injured by the high-energy protons is increased. The RBE value for the protons with an energy of 630 MeV, evaluated according to the criterion of "interphasal destruction", certainly must be greater than one /422
unit. An indication of this is the presence of destructive processes during the early periods after the proton irradiation in doses of 700 and 1100 rad, which are absent or concealed as a result of the low intensity in the case of the effect of γ-rays from Co^{60} in a dose of 700 rad.

As we already mentioned, in addition to the "interphasal destruction", the integral process of radiation destruction can also be augmented by the destruction of the cells formed as a result of aberrant mitosis. On the basis of the RBE value for the protons with an energy of 630 MeV determined by the genetic effect, and according to the results of studying the reproductive destruction of the aberrant cells, we can expect that, for the effect of γ-radiation and the protons in various doses, the rate of which the cells die off because of genetic causes will be less in the case of the proton irradiation. Since it seems impossible to make any reliable determination of the relative degree of participation of each destructive mechanism, we can only emphasize that the RBE value for the protons with an energy of 630 MeV determined according to the intensity of the destructive processes must be included among the RBE values which correspond to the genetic effect and the "interphasal destruction". Rough semi-quantitative evaluations of the RBE in this case give a value which is close to a unit, or which somewhat exceeds a unit. We could also draw the same conclusion from a direct analysis of the changes in the number of cells within the field of vision.

DISCUSSION

According to a widely accepted point of view [21], both genetic mutations and chromosome aberrations are local reactions to one or several ionizations, as a result of which the genetic effect of any type of radiation is determined, essentially, by the linear loss of energy (LLE) of the given type of radiation and the genetic structure of the object being examined. In contrast to this, the physiological effect of radiation, one of the phenomena of which is the reversible suppression of cell division and the "interphasal destruction" of the cells, is not localized at that point in the cell where the ionization occurred It is caused by changes in the chemical structure of the cell as a whole, and is determined by the total amount of energy absorbed by the cell. Obviously, the RBE values evaluated by the genetic and physiological effects of radiation can differ greatly from one another.

It is well known that an increase in the specific density of ionization from 3 to 100 pairs of ions per 1 μ range is scarcely reflected in the RBE value, which remains roughly equal to one unit [252. The unit ionization of protons with an energy of 120 MeV is equal to 20 pairs of ions per 1 μ range, and that of protons with an energy of 660 MeV is equal to 6 pairs [8]. Taking this into account, and considering the relative uniformity of the genetic structures in the cells of mammals, we can expect that the RBE /423
value of the protons evaluated by the genetic effect has practically no relation to the energy of the particles in the range of energies from 120 to 660 MeV. The data available in literature indicate that this is actually so, for the RBE value evaluated by the genetic effect is approximately equal to 0.7 in the range of particle energies being examined. According to data we obtained previously [3] and this study, the RBE values of the protons with energies of 126 and 630 MeV which are evaluated according to the dose-dependence of the relative percentage of chromosome aberrations in the epithelium of the cornea in the mouse practically coincide: they are equal to 0.67 and 0.65, respectively. Similar values were obtained by other authors [8,20] who examined the chromosome aberrations in bone marrow, grains of wheat and barley, and tips of Vicia faba roots, as well as the dominant lethals in fruit-flies. On the basis of an analysis of the chromosome aberrations in bone marrow, N.L. Shmakova [12] gives a value of 0.65 for the RBE of protons with an energy of 660 MeV. A value equal to 0.7 was obtained for the RBE of the protons by G.F. Pal'ga [6] in experiments examining the aberrant mitosis in a stimulated hepatectomy. Ye. D. Plotnikova and S.I. Strashnenko [7] showed that the RBE value of protons with an energy of 500 MeV calculated according to the frequency of dominant lethals in the spermatozoa of rats is equal to 0.6-0.7.

The evaluations of the RBE for high-energy protons according to the physiological effect of radiation are much less homogeneous. The reason for this, in our opinion, is the complexity of the physiological effect itself, which appears in the form of a large number of phenomena of a more simple nature which change with time. As a result, determination of the criterion which gives a quantitative evaluation of the effect with a sufficient degree of reliability is rather complicated. Such a criterion has still not been found, even for such frequently-examined characteristics as the mitotic activity and the number of cells in the tissues of irradiated animals, in relation to which we can make only approximative evaluations of the RBE by these characteristics. Thus, according to the data of N.L. Shmakova [12], the RBE value for the high-energy protons which is determined by the rate of recovery of the mitotic activity can reach 2.0 [26].

An attempt to standardize the determination of the RBE by the physiological effect of radiation, by means of an exponential approximation of the curves for the recovery of mitotic activity, was described in a study by A.D. Strzhizhovskiy [10]. Despite the disadvantages inherent in this method, he was able to determine the

RBE value with high reliability. The RBE values for protons with energies of 126 and 630 MeV which were obtained by using the above-mentioned method were close to a unit. This means that, in contrast to the genetic effect of radiation, the most substantial factor in the case being examined is the total amount of energy, proportional /424 to the dose of radiation absorbed by the cell, and not the density of the ionization.

In conclusion, let us examine the evaluations of the RBE according to the fatality rate of the irradiated mice during the early periods after the radiational effect. According to the data in the literature [2, 5, 15], it is equal to 0.77 for protons with an energy of 157 MeV, and to 0.5-0.6 for protons with an energy of 660 MeV, i.e., it practically coincides with the values found on the basis of examining the genetic effect of radiation within the range of irradiation doses from 100 to 1000 rad.

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CYTOLOGICAL ANALYSIS OF THE DAMAGE TO THE INTESTINAL EPITHELIUM OF MICE WHICH WERE SUBJECTED TO IRRADIATION BY PROTONS WITH AN ENERGY OF 630 MeV

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ABSTRACT: The problem of the specific features of the effect of high-energy protons on radiation-sensitive tissues, particularly the epithelium of the duodenum, was examined in this study. The examination is of definite interest from the point of view of the remote possibility of irradiation of the astronauts by proton radiation from solar flares.

In a preceding article (see this volume), we described in detail the dose-dependence and dynamics of the mitotic activity, the percentage of chromosome aberrations, and the number of cells in the epithelium of the cornea in mice which were subjected to irradiation by protons with an energy of 630 MeV and by γ-radiation from Co^{60}. The results of the study indicated that despite the high radiation-sensitivity of the mitotic activity and the genetic structures of the cells, the decrease in the number of cells in the tissue was relatively small, even for irradiation in fatal doses. Thus, the epithelium of the cornea was a comparatively radiation-resistant tissue. One of the causes of this is the presence of specific mechanisms which increase the resistance of the epithelium in the cornea to various external effects. In the case of a radiation effect, these mechanisms can greatly compensate for the process of the destruction of cells by radiation. /425

In the light of what we have said above, an examination of the specific features for the effect of high-energy protons on radiation-sensitive tissues is of substantial interest. The epithelium of the intestine is a very convenient model for this. It is well known [4, 8, 13] that injury to the intestine is one of the characteristic signs of radiation sickness, while for irradiation within the range of doses from 1 to 10 krad it determines its trend and the end results. In this article, we are presenting the results of studying the biological effect of protons with an energy of 630 MeV on the epithelial cells in the duodenum of the mouse.

METHODS

The examinations were conducted on mice of the CC57br strain. The experimental animals were irradiated totally by protons with an energy of 630 MeV on the synchrocyclotron at Dubna in doses of 200,

700, and 1100 rad. The dose rate was equal to 31.9 rad/sec. The irradiated animals were decapitated simultaneously with the controls, 6 hours, 1, 3, 6, and 9 days after the irradiation. The decapitation was always done at noon, when the mitotic index for the intestinal epithelium was close to its average value per day (5-8). The sections of the duodenum were placed in Carnot solution and then poured into paraffin. Then we prepared sections from them (with a thickness of 5 μ), which we stained with hematoxylin according to Karachi.

For the cytological analysis, we used the following criteria: (1) the number of epithelial cells along the midline of a crypt and a villus; (2) the mitotic index for the epithelium of the crypt; /426 (3) the relative percentage of aberrant mitoses (bridges and acentric fragments) at the stage of the late anaphase or early telophase. The calculation methods were described in greater detail in a study by I.B. Smirnova [5]. For each animal, we calculated the number of cells in 10 crypts and villi, as well as the number of mitoses in 50 crypts, after which we calculated the average number of cells and the mitotic index of a crypt.

RESULTS

The average number of cells along the midline of the crypts in the control animals was equal to 63.2 ± 1.5. The analogous value for the villi was equal to 222.7 ± 2.2. The mitotic index for the epithelium of the crypts in the control mice was equal to $(37.9 \pm 1.9) \cdot 10^{-3}$, and the relative percentage of aberrant mitoses was 0.008 ± 0.005 (Table).

DOSE-DEPENDENCE AND DYNAMICS OF THE CYTOLOGICAL PARAMETERS FOR THE EPITHELIUM OF THE DUODENUM IN MICE WHICH WERE SUBJECTED TO IRRADIATION BY PROTONS WITH AN ENERGY OF 630 MeV

Dose, rad	Time between Irradiation and Decapitation	Mitotic Index of the Epithelium of the Crypts, %	Relative Amt. of Aberrant Mitoses	No. of Cells along the Midline of a Crypt	No. of Cells along the Midline of a Villus
Control		37,9±1,9	0,008±0,005	63,2±1,5	222,7±2,2
200	6 hours	30,1±2,5	0,327±0,027	64,3±1,8	212,9±0,9
	1 day	27,8±0,9	0,278±0,026	55,7±2,5	206,4±3,6
	3 days	36,0±1,9	0,265±0,015	66,7±1,4	209,7±2,2
	6 days	35,0±2,4	0,250±0,021	60,4±2,0	206,6±2,8
	9 days	44,0±2,1	0,194±0,022	66,7±2,6	216,4±3,2
700	6 hours	4,8±0,2	0,896±0,065	52,7±1,5	196,7±2,6
	1 day	24,0±1,4	0,646±0,013	41,2±1,3	207,5±3,3
	3 days	42,7±3,2	0,282±0,024	68,6±2,0	58,0±2,5
	6 days	16,2±1,3	0,308±0,088	65,4±2,8	181,4±8,5
1100	6 hours	2,8±0,4	1,000	53,2±1,6	211,4±4,0
	1 day	17,6±1,5	0,817±0,056	34,8±1,7	199,5±2,7

Knowing the mitotic index and the average duration for the mitosis of a tissue which is in equilibrium, we can determine the average time for its restoration. For the crypts peculiar to the epithelium in the duodenum of the control mice, the mitotic index was $37.9 \cdot 10^{-3}$, and the average duration for the mitosis was about 18 min [6], while the average recovery time was approximately equal to 8 hours. Similar calculations were obtained previously in experiments using radioactive labelling [9, 12]. Thus, each hour, $\frac{63.2}{8} \simeq 8$ cells of the midline of a crypt migrate to a villus, while /427 the new cells arising during the process of cellular reproduction replace them. Since a crypt is in equilibrium with a villus, roughly 8 cells along the mid-line of the latter also must die off in an hour. Obviously, for renovation of all 222.7 cells along the mid-line of a villus, $\frac{222.7}{8} \simeq 28$ hours are necessary. The lifetime of a cell, from the moment of its appearance to the moment of desquamation into the lumen of the intestine is, on the average, equal to 8 + 28 = 36 hours.

On the basis of the data in the literature [10, 14], we can expect that the irradiation of the animals in the dose range being examined will cause almost complete suppression of the mitotic activity immediately after the radiation effect. The curves for recovery of the mitotic activity in the intestinal epithelium of the irradiated mice obviously consist of segments with an initial increase, a repeated drop, and then a subsequent final recovery [14].

From the data shown in the table, we can easily establish that the mitotic activity in the intestinal epithelium of the mice which underwent irradiation by a dose of 200 rad is practically recovered even within 6 hours after the radiation effect. There was probably a repeated drop during the period between the 6th and 24th hours. However, during the following period, there was a final recovery, and (beginning with the 3rd day after the irradiation) the mitotic index for the duodenum of the irradiated mice was the same as the norm.

With an increase in the irradiation dose, the rate of recovery of the mitotic activity decreases. Within 6 hours after irradiation by a dose of 700 rad, the mitotic index for the epithelium of the crypts in the duodenum is only 12.7% of its original value. Normalization occurs on the 3rd day after irradiation. However this is temporary, and it gives way a new drop in the mitotic activity. Within 6 days after irradiation, the mitotic index for the epithelium of the crypts is decreased by more than twice, in comparison with the controls. Irradiation by a dose of 1100 rad causes even greater suppression of the mitotic activity. Within 6 hours after the effect, the mitotic index for the epithlium of the crypts is recovered only by 7.4%, and, after 24 hours, by 46.5%.

In addition to the mitotic activity, the high-energy protons

cause an inhibition of the genetic structures in the cells. This appears visually in the form of chromosome aberrations. From the data shown in the table, we can easily establish that 0.327 of the total number of mitoses observed in the epithelial cells of the crypts are aberrant within 6 hours after irradiation by a dose of 200 rad. The cells with chromosome aberration remain in the tissue for a long time. About 85% of the original number of aberrant cells remain in the tissue for one day, more than 81% remain for 3 days, /428 and roughly 76% remain for 6 days. Even on the 9th day after irradiation, approximately 19% of the cells in the epithelium of the crypts have chromosome aberrations, which is about 60% of the original value. The average value for the mitotic index of the epithelium in the crypts during the period from 6 hours to 9 days after irradiation by a dose of 200 rad is equal to $35.5 \cdot 10^{-3}$, which corresponds to the average duration of a cellular cycle of 8.5 hours. It follows from this that within about one day after irradiation, the cells undergo a second mitotic cycle; and within 3 days, they undergo eight. Within 6 days, they accomplish sixteen mitotic cycles and within 9 days, they finish twenty-five. Thus, only 15% of the aberrant cells divide from 2 to 8 times, 5% from 8 to 16 times, and 16% from 16 to 25 times; finally, about 60% of the aberrant cells divide more than 25 times. It is obvious that the genetic damage occurring in the epithelial cells of the crypts of the duodenum in the mice after irradiation by a dose of 200 rad has a weak effect on the reproductive capacity of the cells.

A different picture can be observed when the animals are given a dose of 700 rad: the cells with chromosome aberrations are eliminated much more rapidly from the tissue. It was shown above that for a mitotic index of $37.9 \cdot 10^{-3}$, the duration of the cellular cycle for the epithelium of the crypts is approximately equal to 8 hours. The irradiation causes a suppression of the mitotic activity and a corresponding increase in the duration of the cellular cycle. The average value of the mitotic index for the first 24 hours after the irradiation is equal to $11.4 \cdot 10^{-3}$, which corresponds to a duration for the mitotic cycle of 26.2 hours. Thus, the cells undergo the first mitosis after irradiation during this period, while the changes in the relative percentage of chromosome aberrations reflect the differences in the radiation sensitivity for the sequential stages of the mitotic cycle. We can see from the data in the table that 0.896 of the total number of cells which are at the later stages of the mitotic cycle during (and are therefore the first to undergo mitosis) have damage in the genetic structures. Of the cells which were at earlier stages of the mitotic cycle during irradiation, only 0.646 were damaged. The relative percentage of cells with chromosome aberrations, averaged over the mitotic cycle, was equal to 0.771.

During the period between the 1st and 3rd days, when the cells pass from the 2nd to the 6th mitotic cycle after irradiation, the relative percentage of aberrant mitoses decreases to 0.282. Thus, $\frac{0.771 - 0.282}{0.771} \cdot 100 = 63\%$ of the aberrant cells do not divide more

than 6 times. For irradiation by a dose of 200 rad, after an equal number of divisions, less than 19% of the aberrant cells are destroyed during reproduction. /429 It follows from this that with an increase in the irradiation dose both the number of injured cells and the degree of injury to their genetic structures increase.

As we can easily establish by evaluating the average value for the mitotic index, during the first day after irradiation by a dose of 1100 rad, only some of the epithelial cells in the crypts can undergo first mitosis. In this case, all the mitoses observed within 6 hours after the effect were aberrant. By the end of the first day, the relative percentage of chromosome aberrations decreased to 0.817. The value for the relative percentage of aberrant cells averaged over the part of the mitotic cycle being examined was equal to 0.908. Having compared the levels of chromosome aberrations in the first mitosis for the epithelial cells of the duodenum after irradiation by doses of 200, 700, and 1100 rad, we can easily establish that the dose-dependence for the genetic effect of the protons with an energy of 630 MeV is exponential in the dose range being examined. The average effective dose was equal to 480 rad.

Let us examine further the results of measuring the number of cells along the midline of a crypt. From the data shown in the table, we can see that, within one day after irradiation by a dose of 200 rad, there is a decrease in this characteristic, roughly by 12%. By the 3rd day, the number of cells in the crypt has recovered and remains normal up to the end of the study. For irradiation by a dose of 700 rad, the radiation effect is much more pronounced. Within 6 hours after the effect, the number of cells in a crypt decreases by 17; within 24 hours, it decreases by 35%. However, there is a recovery of this characteristic during the following periods, which is completed by the end of the 3rd day. During the period between the 3rd and 6th days after the irradiation, the number of cells in a crypt remains normal. With an increase in the dose of irradiation to 1100 rad, the degree of injury to the epithelial cells of the crypts increases even more. The number of cells along the midlines of the crypts decreases by 16% within 6 hours after the irradiation, and by 45% within 24 hours.

Among the factors which can cause a decrease in the number of cells in the epithelium of the crypts in the duodenum of irradiated animals, the most important, in our opinion, are the decrease in the rate of formation of new cells because of the suppression of the mitotic activity, and the destructive processes occurring in the cells with radiation damage. On the basis of the results from a study of the physiological regeneration of the intestinal epithelium in normal mice, we can exclude the first possibility. As we noted earlier, the average lifetime for the cells in the epithelium of the duodenum in a mouse is equal to 36 hours: the cell is in a crypt for about 8 hours, and in a villus for 28 hours. From this, we can expect that, in the case of a complete suppression of the

mitotic activity, when the cells of a crypt are not displaced to a villus, they will begin to die off naturally because of age no earlier than 28 hours after the mitotic activity was blocked. In addition to this, even for a complete suppression of the mitotic activity, the number of cells along the midlines of the crypts in the duodenum of the mice which were irradiated by doses of 700 and 1100 rad is decreased even within 6 hours after the radiation effect. This shows the existence of the intense process of radiation destruction of the cells. /430

The number of cells along the midline of a villus was decreased for 6 days after irradiation by a dose of 200 rad. However, this decrease was small, and it reached a maximum at only about 7% of the original number of cells. On the 9th day, there was no statistically reliable divergence observed for this characteristic from the normal value. We observed a decrease in the number of cells in the villus, which was similar in value for the first day after irradiation by a dose of 700 rad. The number of cells along the midline of a villus then dropped sharply and reached 26% of the original value by the 3rd day. During the following period, this characteristic was gradually restored, and it was only 18% lower than the norm on the 6th day after the irradiation. It is interesting to note that the minimum number of cells in a villus is observed when the number of cells in a crypt has already normalized. During the first day after irradiation by a dose of 1100 rad, there is also a very rapid decrease in the number of cells in the villi. While the number of cells along the midline of a crypt decreases almost by a factor of 2, a similar characteristic for the villus is decreased only by 10%.

In order to clarify the causes for the leveling-out of the villi after irradiating the animals with doses which were close to lethal, it is useful to examine in greater detail the scheme for regeneration of the intestinal epitheliu. As we mentioned earlier, the entirety of the villi is maintained because of the cells coming from the crypts. The reason for this is the displacement of the cells in the crypts to the villi, caused by cellular reproduction. In normal crypts, the intensity for migration of the cells is proportional to the mitotic index for the epithelium of the crypt. If the number of cells in a crypt is less than the norm, then the displacement of the cells to the villus does not occur before its normalization.

On the basis of what we have said, we can expect that on the first day after irradiation by a dose of 700 rad, the migration of the cells from a crypt to a villus is practically absent. Nevertheless, the number of cells along the midline of a villus diminishes during this period roughly by 10%. If the displacement of vital cells from the villi of the intestinal epithelium in normal mice were absent, and the natural lifespan of a cell in a villus were equal to the time for its recovery in the process of physiological regeneration, i.e. 28 hours, then even when there is no radiation

destruction of the cells, the decrease in the number of cells in the villus would be much more intense during this period. It follows from this that in the intestinal epithelium, as well as in the /431
epithelium of the cornea, the displacement of vital cells stabilizes the tissue in relation to various external effects. The potential lifespan for the cell exceeds the real duration of its existence, obviously, by more than one day but less than 3 days, since the number of cells along the midlines of the villi has decreased considerably by the 3rd day after irradiation. Thus, in order to explain the leveling-out of the villi after the animals were irradiated in doses which were close to lethal, we do not need to postulate the existence of radiation destruction of the cells in a villus, although this possibility is definitely not excluded. In our opinion the principal cause for the leveling-out of the villi in this case is the temporary cessation of the migration of the cells from the crypts to the villi.

DISCUSSION

Having compared the materials of this study with the results of studying the radiation injury to the epithelium of the cornea, we can shed some light on certain reasons for the high radiation-sensitivity of the intestinal epithelium. In these studies, we analyzed the blocking and recovery of the mitotic activity, the appearance and dynamics of chromosome aberrations, and the destruction of the cells in the irradiated tissues.

On the basis of determining the high radiation-sensitivity of the intestinal epithelium, we find that for irradiation of equal doses, the number of cells along the midlines of the crypts and villi decreases much more than the number of cells in radiation-resistant tissues such as the epithelium of the cornea. The reason for this, as we showed before, is the intense radiation-produced destruction of the cells in the crypts and the related temporary cessation of the migration of the cells from the crypts to the villi. However, the nature of the destructive process occurring in the cells of the crypts and the causes for the much greater (in comparison with the epithelium of the cornea) devastation of the villi are still rather unclear.

Judging by the data in the literature [10, 14], the irradiation in the range of doses being examined causes a complete suppression of the mitotic activity of the epithelium in the duodenum and in the cornea. However, the restoration of this characteristic after irradiation in equal doses occurs much more actively in the intestine than in the cornea. We should expect this, since the total rate for the recovery of mitotic activity combines the rate of intracellular recovery and the rate of replacement of injured cells by normal ones appearing as a result of multiplication by uninjured and recovered cells [7]. The latter component, which obviously increases with an increase in the mitotic activity of uninjured /432
cells, is much greater in the case of the intestinal epithelium.

It follows from this that the mitotic activity of the epithelium in the crypts of the duodenum, generally speaking, is more radiation-resistant than the mitotic activity of the epithelium in the cornea.

Having compared the levels of chromosome aberration in the first mitosis of the cells for the epithelium of the cornea and the intestine, we can easily be convinced that the genetic structures of these two types of cells have a similar radiation sensitivity. The average effective dose for the genetic effect of irradiating the epithelium in the cornea by protons with an energy of 630 MeV is equal to 540 rad, while it is 480 rad for the epithelium of the intestine. However, an injury to the genetic structure affects the reproductive capacity of the cells in these tissues to varying degrees. For example, the aberrant cells of the epithelium in the cornea which are formed after irradiation by a dose of 200 rad divide roughly twice or less, and the reproductive disintegration of the cells, obviously, is often accompanied by cellular destruction. At the same time, about 60% of the aberrant cells formed after irradiation by a dose of 200 rad in the epithelium of the crypts in the duodenum divide more than 25 times. This fact of the prolonged preservation and multiplaction of the aberrant cells in the epithelium of the crypts is of substantial interest in the light of the possible remote aftereffects of the radiation effect. Hence, we can also expect that for irradiation in equal doses, the rate at which the cells die off because of a disorder of the genetic balance occurring during the process of aberrant mitosis in the epithelial cells of the intestine will be less than in the cells of the epithelium in the cornea.

Thus, the more intense (by comparison with the epithelium of the cornea) devastation of the crypts and villi in the intestinal epithelium cannot be explained by the suppression of the mitotic activity or the decomposition of the cells related to genetic causes.

The reason for the high radiation sensitivity of the epithelium in the crypts, in our opinion, is the increased intensity of the so-called interphasal destruction of the cells caused by injury to other than genetic intracellular structures. The decreased resistance of the epithelium in the villi in relation to a radiation effect can be related to the lesser (in comparison with the epithelium of the cornea) degree by which the potential lifetime of a cell exceeds the actual time of its existence. This value determines the time for maintaining the entirety of the tissue when no cells come from the proliferative pool. For the cells of the intestinal epitheliu, its value (as we have shown above) is between one and three days, while it exceeds 4.6 days for the cells in the epithelium of the cornea [7].

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EVALUATION OF THE PERMISSIBLE DOSES FOR EXPOSURE TO IONIZING RADIATION ACCORDING TO THE CRITERION OF TOLERANCE TO EXTREME ACCELERATIONS

B.I. Davydov, V.V. Antipov, and P.P. Saksonov

ABSTRACT: The doses of irradiation for which the tolerance of the irradiated animals to acceleration was equal to the control were ob-tai tained by calculations. The doses of irradiation thus obtained were related to the post-radiation period by the hyperbolic function,

$$Dt = 5 \cdot 10^3,$$

where D is the dose of irradiation in rem; t is the time after the irradiation in days.

For centrifuging repeated twice, this relationship could be approximated by an exponential function and represented by the following regression equation:

$$\log D = 2.993 - 0.065 \cdot \log e \cdot t \quad (t \gg 5).$$

The unusual conditions of a space flight (dynamic factors, /433
weightlessness, the altered gaseous composition of the medium in the cabin of a spacecraft, etc.) produce definite difficulties for evaluating the tolerable doses of irradiation. In evaluating the maximum permissible doses for pilots and astronauts, we must first determine an irradiated organism's tolerance to various extreme effects and to the carrying out of work during the space flight.

We can consider that the reactivity of an irradiated organism to the factors of a space flight is other than that in response to the usual effects of the environment. There is an insufficient number of studies on this problem in the literature. Nevertheless, this problem has important theoretical and practical significance.

One of the important factors of an aircraft or space flight is acceleration [15]. We showed earlier [9] that, for the first 6 days after the effect of ionizing radiation, animals react to accelerations in an unusual way (according to the test of the survival rate): their tolerance to this extreme flight factor increases. /434
We found a relationship between the maximum radiation dose at which the effect of an acceleration on irradiated animals was equal to the effect on intact ones, and the time between the irradiation and the effect of acceleration [10].

In this article, we provide an experimental confirmation of the extrapolated segment of the curve for the tolerance to accelerations, for various doses of radiation during various periods after the effect of ionizing radiation. Moreover, we have attempted to evaluate the role of the recovery processes in an irradiated organism in its reaction to accelerations which are critical in value.

We are presenting certain concepts which show the possibility for extrapolating the experimental data for a human being, and for obtaining the oriented data on the permissible doses of irradiation evaluated according to the criterion of tolerance to acceleration.

METHODS

The experiments were performed on 1200 white mice (males of no particular strain) and on 120 mice of the CC57br and CBA strains and hybrids of the first generation of C57bl*CBA. The death of the animals was the test which determined the reactivity of the animals (after the effect of ionizing radiation) to accelerations.

The mice were irradiated with the RUM-11 apparatus under the following conditions: Al = 1 mm, Cu = 0.5 mm, 180 kV, 10 ma. Some of the animals were subjected to γ-irradiation from Co^{60}. The dose rate was 15-18 r/min. The doses for irradiation of the animals were the following: 100, 200, 250, 300, 350, 500, 700, 850, 900, 2000, and 4000 rem.[1] From the first to the forty-fifth days after irradiation, the animals were subjected to the effect of an acceleration of 44 g for 3 min in the "back-chest" direction, with a lift and drop lasting 30-50 sec. In one series, the animals were placed in a centrifuge with a radius of 0.31 m. In this case, the angular acceleration was rather high. Under these conditions, the stress killed approximately 50% of the control mice. In the remaining series, the animals were placed in a centrifuge with a radius of 4.2 m. In order to study the reaction of the irradiated animals to repeated accelerations, the centrifuging was conducted with the same parameters, 10 min after the first effect of an acceleration.

RESULTS AND DISCUSSION

The tolerance of animals to accelerations during various periods after irradiation depends on the dose, and can be represented by a hyperbolic curve (Fig. 2). The results of these studies are given in Table 1 and Figure 1. As we can see from Figure 2, the segment of the curve where $1 < t < 9$ conforms fairly well with the /43
experimental values. In addition to this, we tested the validity of this relationship for the more remote periods of radiation sickness, and obtained the experimental data on the tolerance to accelerations during the first days after the irradiation.

[1]The RBE (relative biological effectiveness) for the γ-rays was 0.75 [19].

TABLE 1. DEATH OF MICE FOLLOWING THE EFFECT OF ACCELERATION AFTER X-RAY IRRADIATION IN DOSES OF 250-850 REM

Dose, rem	No. of Animals	Interval between Irradiation and Centrifuging	Centrifuging			
			First		Second	
			abs.	%	abs.	%
Control	40	3	17	42	30	75
250	40		18	45	28	70
Control	40	5	23	58	32	80
250	40		15	38	28	72
Control	40	9	19	47	32	80
250	40		23	58	31	78
Control	27	1	10	40	17	63
500	20		6	30	16	59
Control	40	2	20	50	28	70
500	40		17	42	18	45
Control	42	5	18	43	26	62
500	38		9	24	16	42
Control	39	9	18	43	25	64
500	40		21	53	24	60
Control	40	3	15	37	19	48
700	40		10	25	19	48
Control	43	5	28	65	36	84
700	40 (3)		21	56	26	70
Control	28	9	7	25	14	50
700	38 (18)		7	35	15	75
Control	60	1	33	55	37	62
700	100		44	44	76	76
Control	16	2	9	56	15	94
850	16		4	25	12	75
Control	35	8	15	43	—	—
850	41 (22)		7	37	—	—

NOTE: The number of animals which died after irradiation is given in parentheses.

The original segment of the curve in Figure 2 assumes the presence of the tolerance of the mice to accelerations for a dose on the order of 4000 rem. With a certain degree of reliability, we can /436 assume that any point in the shaded segment of Figure 2 reflects the irradiated animals' tolerance as being greater than or equal to the control. For example, for irradiation by doses of 2000 and 4000 rem, the animals' tolerance to accelerations on the first day after the effect should be the same as in the controls, or somewhat higher.

Table 2 shows the data for the determination of the tolerance of the mice to acceleration on the first day after γ-irradiation in doses of 2000 and 4000 rem. The animals were subjected to the effect of an acceleration of 44 g, repeated twice for 10 min with a pause of 10 min, on a centrifuge with a radius of 3 m. As we can

see, the tolerance of the animals to the acceleration was higher than for the control mice: A/A_0 = 0.86 and 0.58, respectively, for 2000 and 4000 rem.

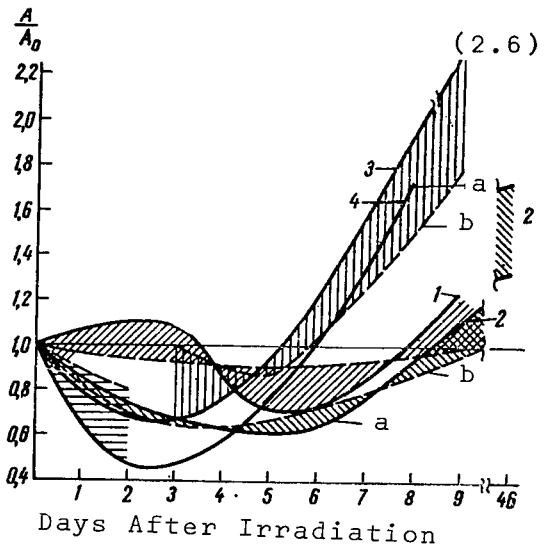

Fig. 1. Tolerance of Irradiated Mice to Acceleration. (1) 250 rem; (2) 500; (3) 700; (4) 850 rem; (a) Single Centrifuging; (b) Centrifuging Repeated Twice; (A) Death (%) of Experimental Animals; (A_0) Death of Controls

After repeated centrifuging, the mortality rate for the irradiated animals was 56% for a dose of 2000 rem, and 70% for 4000 rem. It is well known that the average lifespan for mice after doses of 1500-15,000 rem is roughly 3.5 days [16]. With an increase in the radiation dose beyond 15,000 rem, the average lifespan begins to decrease rapidly. We can assume that the animals' tolerance to an acceleration at t < 1 will remain within the limits of the control level for doses on the order of 10,000-15,000 rem. /437

As we said earlier, the curve in Figure 2 was obtained by determining the margin of tolerance for the animals to acceleration, for 9 days after the radiation effect. The segment of the curve where t > 9 days after the irradiation had to be tested experimentally.

TABLE 2. DEATHS OF MICE AFTER THE EFFECT OF AN ACCELERATION, DURING THE FIRST DAY AFTER γ-IRRADIATION IN DOSES OF 2000 and 4000 REM.

Group	Number of Animals	Number of Animals which Died After the Effect of the Acceleration	
		First Effect	Second Effect
Control	14	4 (29)	10 (71)
2000 rem	16	4 (25)	9 (56)
Control	20	12 (60)	13 (65)
4000 rem	20	7 (35)	14 (70)

NOTE: The percentages of the original data are given in parentheses.

The animals which were irradiated by doses of 100, 200 and 350 rem were subjected to the effect of an acceleration on the 45th day, while those irradiated by doses of 300 and 500 rem underwent acceleration on the 16th day after irradiation. The centrifuging was repeated 3 times, and was 44 g for 5 min with a pause of 8-10 min (Table 3). By the method of graphical interpolation-extrapolation of the curves in Figure 3, we could determine the doses for which the effect on the experimental animals was equal to that for the control. It is obvious that in determining the tolerable dose of irradiation, we had to make a definite assumption regarding the linear relationship between the animals' reaction to the acceleration and the value for the radiation dose within the range of the experimental doses. During the earlier periods after irradiation, this relationship is more complex [9].

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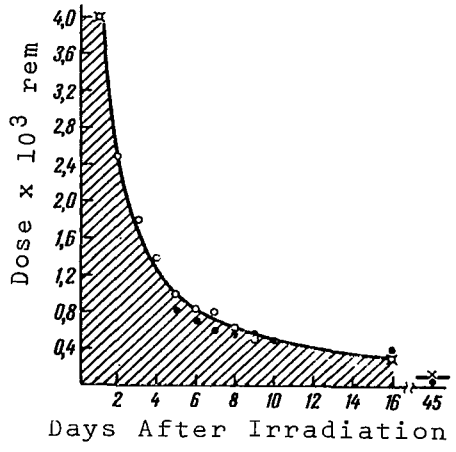

Fig. 2. Dose-Time Curve for the Resistance of the Irradiated Mice to Acceleration.

TABLE 3. DEATHS OF MICE AFTER THE EFFECT OF AN ACCELERATION, ON THE 16th AND 45th DAYS AFTER IRRADIATION BY VARIOUS DOSES

Group*	Centrifuging					
	First		Second		Third	
	abs.	%	abs.	%	abs.	%
After 45 days						
Control	5	25	8	40	9	45
100 rem	6 (6)**	24 (30)	8 (9)	47 (45)	9 (10)	48 (50)
200 rem	2 (8)	14 (40)	4 (10)	29 (50)	8 (12)	57 (60)
350 rem	5 (11)	36 (55)	7 (13)	50 (65)	10 (16)	71 (80)
After 16 days						
Control	7	35	10	50	13	65
300 rem	1 (7)	7 (35)	1 (7)	7 (35)	1 (7)	7 (35)
500 rem	8 (12)	50 (60)	9 (13)	56 (65)	9 (13)	56 (65)

NOTE: *Twenty animals in each group.

**The number of animals which died from irradiation + acceleration is given in parentheses.

The doses for which (on the 16th and 45th days after irradiation) the animals' tolerance to the acceleration corresponded to the control, averaged 481 and 150 rem, respectively. Taking the deaths from irradiation into account, these doses were somewhat lower: 400 and 85 rem.

Thus, the experimental data obtained show that the degree of resistance on the part of the mice to acceleration depends on the radiation dose. This dependence can be described by the following equation:

$$Dt = 5 \cdot 10^3, \qquad (1)$$

where D is the dose in rem; t is the time after irradiation in days.

All of the above refer to an acute single irradiation. Obviously, for a fractionated irradiation, we must consider the processes of post-radiation recovery.

According to the theories of Blair and Davidson [20, 11], the post-radiation recovery processes can be expressed by the following /439
equation:

$$D_e = D_i[f + (1 - f)e^{-\beta t}], \qquad (2)$$

where D_e is the effective radiation dose; D_i is the dose of irradiation; f is the irreversible part of the damage; t is the number of days; β is the recovery rate; e is the base of the natural logarithm.

For mice, according to the data of Paterson et al. [33], the period of half-recovery lasts 5.5 days, for a recovery rate equal to 12.5% per day. We assumed that the tolerance of irradiated animals to acceleration can depend (obviously) on the degree of the radiation effect, considering the post-radiation recovery. If the reaction to an acceleration depends only on the irreversible part of the radiation damage, then for repeated irradiation the doses will be summed according to D_e, and not according to D_i.

For example, the calculations show that, for an irradiation /440
repeated twice at doses of 600 rem with an interval of 5 days, D_e has a total of about 744 rem on the second day after the second effect. In the calculations, we took f as equal to 0.1 (10%). If we then subject the irradiated animals to centrifuging, we can expect that their tolerance to acceleration will be the same as for a single irradiation at the same dose. The experiment was conducted roughly by such a scheme. Simultaneously with a group of animals which were irradiated twice at a dose of 660 rem, we irradiated another group once at a dose of 850 rem (the D_e on the second day after irradiation is roughly 700 rem) (Table 4).

TABLE 4. DEATHS OF MICE AFTER THE EFFECT OF ACCELERATION, AFTER IRRADIATION REPEATED TWICE (600 rem x 2), AND AFTER A SINGLE IRRADIATION (850 rem)

Group	Number of Animals	Interval between Irradiation and Centrifuging, days	Number of Animals which Died After Centrifuging
600 x 2	18	2*, 7**	6 (33)***
Control	22	-	12 (54)
850	16	2	4 (25)
Control	16	-	9 (56)
850	41 (22)	8	7 (37)
Control	35	-	15 (43)

*After a Second Irradiation.

**After a First Irradiation.

***The Percentages of Deaths from Irradiation are in Parentheses.

The experiment conducted according to this scheme takes into account the fact that the restoration processes in an irradiated organism can be clarified according to the criterion of the tolerance to extreme acceleration.

There are general rules among the reactions of irradiated animals to extreme acceleration and repeated irradiation. There are periods of increased and decreased sensitivity of the irradiated animals to acceleration and repeated irradiation. The period of the animals' increased resistance to acceleration, according to our data, is equal to 8-9 days for doses of 250-500 rem. The period of increased radiation-resistance, determined by the test of repeated irradiation, corresponds roughly to 12-15 days [1].

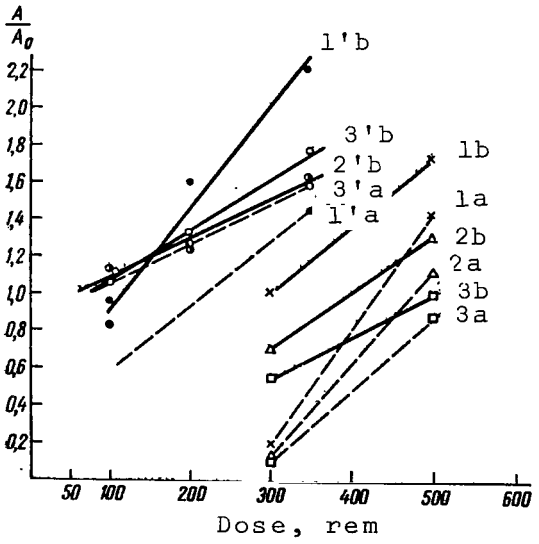

Fig. 3. Relationship between the Tolerance of the Mice to Acceleration and the Dose of Irradiation. (1, 2, and 3) Centrifuging 16 Days After Irradiation; (1', 2', and 3') Centrifuging 45 Days After Irradiation; (a) Deaths After the Effect of an Acceleration; (b) Deaths After the Effect of Irradiation and Acceleration; (A and A_0) Same as in Figure 1.

Certain authors [2] have noted in mice an increased or normal resistance to strychnine and novoembichine in Erlich's tumors, even 50-65 days after irradiation. This contradicts Blair's theory [20] on the presence of an irreversible component in the radiation damage.

On the other hand, the data we obtained indicate that on the 45th day after the irradiation there is an irreversible component in the radiation damage which is found by this test. /441

It is interesting to note certain differences in the tolerance to accelerations after the effect of ionizing radiations in the mice of a particular strain. Thus, on the first day after irradiation by a dose of 900 rem, the apparent sensitivity of the mice of the strains CC57br, CBA, and C57blxCBA to the effect of an acceleration is rather even. If, in the control, the deaths (in %) after accelerations for the hybrids C57bl CBA-50, CC57br-65, and CBA are 90%, then, after the irradiation of C57bl x CBA-65, CC57br-75, and CBA, they are 70%. The radiation factor seems to take away the natural differences in the sensitivity of the mice to accelerations. It is interesting to note that the radiation-sensitivity of the CC57br strain is higher ($LD_{50/30}$ = 538 rem) than for CBA ($LD_{50/30}$ = 748 rem) [14], while the sensitivity to accelerations is higher for the CBA strain.

Let us now attempt to evaluate the tolerance of the irradiated animals to the repeated effects of critical accelerations. This is of interest in determining the tolerable doses by means of repeated effects. It is certain that each effect changes the reactivity of an animal. Therefore, it is interesting to know how and in what way the reaction of an organism changes with respect to the repeated effect of the same factor. Therefore, the repeated effect of accelerations at a certain interval after the first centrifuging will be our test for the reactivity of the animals which remain alive.

If A_0^1 and A_0^2 are the numbers of deaths (%) of the control animals, while A^1 and A^2 are the same for the irradiated animals, corresponding to a first and second centrifuging, then $A^1/A_0^1 = K_1$ (the index for the tolerance to a first acceleration) and $A^2/A_0^2 = K_2$ (the index for the tolerance to a second acceleration). When $K < 1$, the resistance of the irradiated animals to accelerations is higher; when $K > 1$, it is lower.

We can assume that the reaction of the irradiated animals to repeated centrifuging is a function of the period of the radiation sickness.

The curves plotted in Figure 4 for doses of 250 and 500 rem are K_1/K_2 at various days after the irradiation. These curves were obtained by analyzing the data shown in Figure 1. As we can see

from Figure 4, on the 4th to 7th days after the irradiation, $K_1/K_2 < 1$, i.e. the tolerance of the irradiated animals during the repeated acceleration is lower than during the first effect. During the remaining periods, it was found (on the other hand) that the resistance of the irradiated animals to the second centrifuging was higher than for the first. For a dose of 100 rem, K_1/K_2 is almost equal to 1. Therefore, we can consider that, for a dose of 100 rem, the animals react to the repeated centrifuging in the same way as the controls.

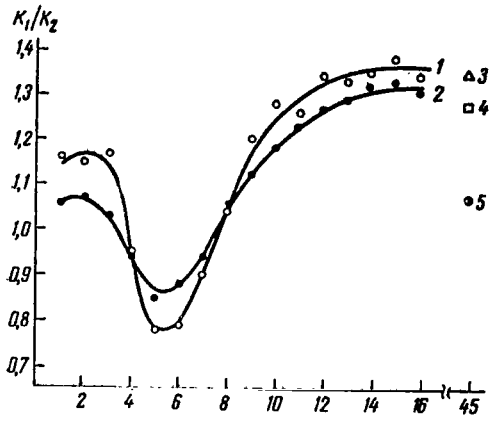

Fig. 4. Ratio of the Indices for Tolerance (K_1/K_2) to Accelerations for Mice during Single and Repeated Centrifuging. (1) 500; (2) 250; (3) 350; (4) 200; (5) 100 rem.

The tolerable radiation doses for the animals during a second centrifuging can be determined by analyzing the data in Figure 3. The results of this analysis are shown in the form of four small circles in Figure 2. As we can see from this Figure, the permissible radiation doses are somewhat lower for a second centrifuging than for one effect of an acceleration. When $t \gg 5$, the data on the tolerance of the irradiated animals to repeated accelerations can be approximate by the following exponential function $D = D_0 e^{-\alpha t}$, where D is the dose in rem; D_0 is the initial dose in rem; t is the time after the irradiation in days; e is the base of the natural logarith; α is a coefficient. /442

By an analysis according to the method of least squares, we obtained the following regression equation:

$$\log D = 2.993 - 0.065 \cdot t \cdot \log e; \quad (t \gg 5). \qquad (3)$$

EXTRAPOLATION OF THE DATA OBTAINED FOR A HUMAN BEING

Previously [9], on the basis of comparing the data for mice on the tolerance to acceleration and the dynamics for the decrease in the number of leukocytes after irradiation by a dose of LD_{50} in human beings and animals, we attempted to determine the period for half-recovery of the normal reaction of an organism to the effect of an acceleration.

The periods for half-recovery of radiation-resistance, determined by the method of repeated irradiation [11] differ little from

the tolerance of the mice to extreme acceleration [9], and for a dose of about DL_{50}, they last about 5-6 days in both cases. For a human being, the period of half-recovery was determined as 25-35 days, which agrees with the data of other authors, who obtained these values by other methods [11].

However, we should note that only the half-period for the decreased sensitivity of the irradiated animals corresponds to the half-recovery period determined by the test of repeated irradiation.

Before obtaining the curve for the tolerance of a human being to extreme acceleration after various doses of radiation, we should attempt to select the corresponding criteria for obtaining the extrapolated coefficients. One of the criteria by which we can obtain the extrapolation coefficient is the difference in radiation sensitivity for men and animals. On the basis of the data on the $LD_{50/30-60}$ [4, 12, 16, 25, 28, 29, 32, 34], we obtained the curves for the fatal effects for human beings and mice. As we can see from Figure 5, the coefficient of radiation sensitivity for mouse or human averages 1.35 according to the fatality rate, for levels of probability of 0.1-0.95%. /443

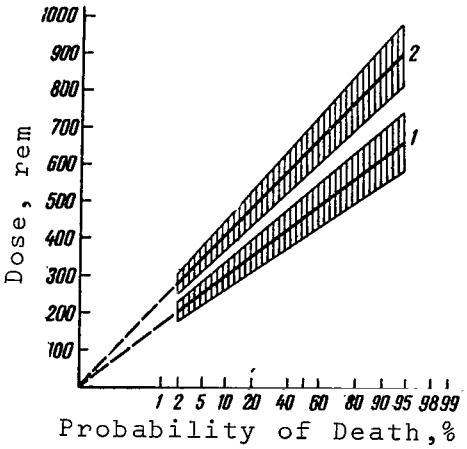

Fig. 5. Probability of Deaths From Various Doses of Radiation, for a Human Being (1) and for a Mouse (2)

It was shown earlier that the curve for the tolerance of irradiated mice to accelerations agreed with the average lifespan of the irradiated mice [9]. We can consider that this interrelationship is preserved for a human being. Actually, the period of normal (or decreased) sensitivity of an irradiated organism to accelerations can not be more than the average lifespan.

Considering the differences in the average lifespan after irradiation of a human and a mouse, we can obtain the corresponding coefficients of extrapolation from animals to human beings for doses of 300-2000 rem (Table 5). For doses of 300-600, 700-900, and 1000-2000 rem, these coefficients are 1.77 (1.72-1.88), 2.00 (1.95 -2.05), and 2.50, respectively. With this coefficient for doses of 300-2000 rem, Equation (1) takes the form $Dt = 5 \cdot 10^3 \cdot L$, where $L_{300-600\ \text{rem}} = 1.77$; $L_{700-900\ \text{rem}} = 2.00$; $L_{1-2\ \text{krem}} = 2.50$; considering the coefficient of radiation sensitivity as equal to 1.35, we find the following:

$$Dt = 3.7 \cdot 10^3 \cdot L \quad (200\ \text{rem} < D \ll 700\ \text{rem}). \qquad (4)$$

For doses less than 200 rem, when the probability of death, according to the data [28], is only 1-3%, it is obviously not necessary to use the coefficient of extrapolation obtained on the basis of the data for the average lifespan.

In our opinion, for doses less than 200 rem, it is necessary to use the criterion of difference in the rates of the recovery processes. It is well known that the rate of the recovery processes after radiation damage correlates with the rate of the metabolic processes, and thus with the type of animal. /444

TABLE 5. RATIO OF THE AVERAGE LIFESPAN FOR A HUMAN (H) AND FOR A MOUSE (M) AFTER IRRADIATION BY DOSES OF 300-2000 rem [16, 28].

Dose, rem	Average Life-span, hours	H/M	Dose, rem	Average Life-Span, hours	H/M
300	750/430	1,75	800	400/200	2,00
400	650/380	1,72	900	330/170	1,95
500	600/320	1,88	1000	300/120	2,50
600	510/290	1,76	2000	210/84	2,50
700	430/210	2,05			

According to the data of a number of authors, the periods for half-recovery of the radiation sensitivity in a human and in a mouse are 25-35 days and about 5 days, respectively. Davidson [11] determined the average period of half-recovery for a human as equal to about 28 days. According to the criterion of tolerance to extreme acceleration, according to our data, it is about 26 days [9]. The ratio for the periods of half-recovery between a human and a mouse is 5.6-5.2.

For 45 days after irradiation by a dose of 100 rem, the tolerance to acceleration is lower than in the controls. According to Formula (2), this period is longer than the period for complete recovery from radiation damage in mice. For a human, the period for complete recovery of the reversible part of radiation damage is equal to 200 days [11]. Thus, in this case the ratio between the periods of complete recovery for a human being and a mouse is about 4.4. The coefficients obtained by various methods are rather close. On the average, this coefficient is equal to about 5. For doses of 200 rem, Formula (4) takes the following form:

$$Dt = 1.85 \cdot 10^4; \quad (D \leq 200 \text{ rem}).$$

Formula (3), which describes the reaction of an irradiated animal to repeated centrifuging, must also be related to the corresponding coefficients of extrapolation for obtaining the curve of the tolerance of an irradiated human being to the repeated effect of acceleration.

Figure 6 shows the data obtained by extrapolation of the normal tolerance to accelerations for a human being who underwent irradiation in doses of 200-700 rem, and for a dose << 200 rem. However, we must consider the time for the primary reaction. Thus, according to the data in the literature, which were combined in a study by Yu.G. Grigor'yev, A.D. Gus'kova, and M.P. Domshlak [7], the pronounced primary reaction for doses up to 400 rem lasts up to 3 days. The probability of the appearance of a primary reaction is related /445
to the dose of radiation received, as we can see in Figure 6 (b) and (c). Certain differences in the data are obviously linked with the fact that some were obtained from people who were irradiated as a result of a disaster or an accident, and others were obtained during therapeutic irradiation of patients.

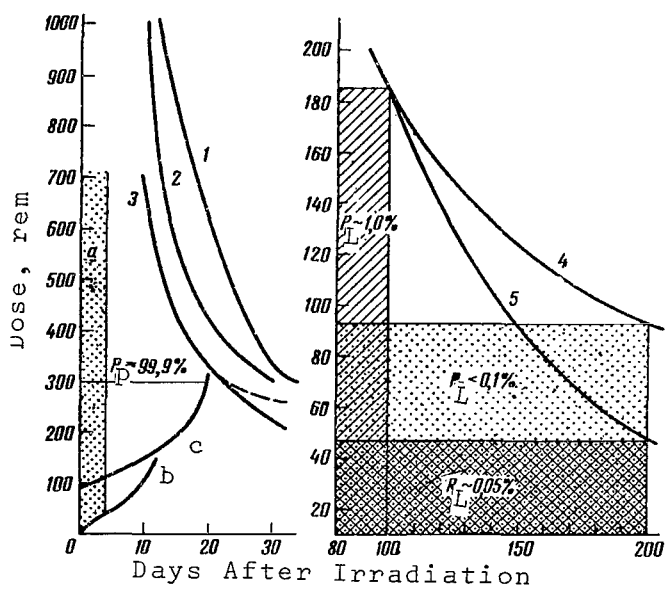

Fig. 6. Calculated Dose-Time Curve of the Resistance of Irradiated Humans to Critical Accelerations (1) Average Lifespan; (2) Tolerance to Accelerations (Coefficient of Extrapolation of the Average Lifespan); (3) Tolerance to Accelerations, Considering the Coefficient of Radiation Sensitivity; (4) Tolerance to Acceleration (Single Effect) for Doses of 200 rem; (5) Same, for Repeated Acceleration; (a) Maximum Period for Primary Reaction [7]; (b) Probability of a Primary Reaction (P_P), % [7]; (c) Same as (b) (for a Dose of 300 rem, P_P = 99.9%) [21-24, 26, 30, 31]; (P_L) Probability of a Lethal Result [28].

As we can see from Figure 6, the radiation dose is functionally linked with the time after the irradiation. In order to determine the minimum dose of irradiation for which the tolerance to acceleration is normal, we must determine that period which could be taken as the final point on the scale of the abscissa in Figure 6.

Therefore, we must select the criterion which would determine this temporary point. For the final point on the axis of the abscissa in Figure 6, with a definite allowance, we can take the interval which is equal (first of all) to the first half of the period for complete post-radiation recovery, during which there is compensation of 90% of the reversible component of radiation damage, and (secondly) which is equal to the period for complete recovery. According to Formula (2), the period for complete recovery from radiation damage, evaluated according to the recovery of radiation sensitivity, is equal to 200 days. /446

The minimum permissible dose of radiation which does not cause a change in the reactivity of an organism to an acceleration for 200 days is about 90 rem. For repeated centrifuging, this dose is equal to about 50 rem.

Thus, on the basis of our data, obtained by extrapolation, we can assume that, for doses of 50-90 rem, the tolerance of a human being to accelerations at any time within 200 days after irradiation within the limits of these doses is obviously the same as for a healthy person.

CONCLUSION

The problem of determining the permissible doses of ionizing radiation for the crew members of aircraft has been discussed in a number of studies [6, 18, 27]. However, in most cases the criteria which the authors used for evaluating the permissible doses were inadequate for space flight.

Therefore, it seemed interesting to attempt to analyze certain other methods for evaluating the permissible doses which would be more specific for the factors of a space flight. At the first stage, we selected accelerations as the first criterion. In this article, we studied only the partial case of the tolerance to accelerations in an organism which was exposed to ionizing radiation [3, 8]. As was shown earlier [9, 10] and in this article, an animal tolerates the effect of extreme accelerations during the first period after irradiation much better than do the control animals.

On the other hand, the preliminary effect of an acceleration on an organism decreases the radiobiological effect of the ionizing radiation [3, 8].

However, it is possible that for a combination of sub-marginal (or subcritical) stresses (irradiation + acceleration, or acceleration + irradiation), the reaction of an organism to the effect of a third stress (for example, physical and emotional stress, etc.) can be quantitatively and qualitatively different than for the interaction of only two stresses.

Using the quantitative differences in the radiobiological rules

for mice and humans, we attempted to perform an extrapolation of the experimental data for human beings, recognizing the conditionality of such a method. However, we should note that there is a similarity in certain qualitative radiobiological changes for mice and humans. Thus, Mate [12] mentions that a decrease in various different types of cells in the blood of a human being occurs in the same chronological order as for a mouse: first lymphocytes, then reticulocytes, granulocytes, and, finally, thrombocytes. As P.P. saksonov [17], A.S. Mozzhukhin, and F.Yu. Rachinskiy [13] show, a comparison between the clinical pictures of acute radiation sickness for humans and higher animals shows that there are only quantitative differences in its remote symptoms, as well as in the periods of its development after irradiation. /447

It is certain that a number of experiments must be conducted in the future on other types of animals, in order that we may have the possibility for making corresponding clarifications of the extrapolation coefficients obtained.

There should also be an attempt to determine the permissible doses of irradiation while selecting other extremal factors of space flight as the criteria for the calculations.

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THE SURVIVAL RATE OF ANIMALS FOLLOWING GENERAL γ-IRRADIATION WHILE SHIELDING THE ABDOMINAL REGION

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ABSTRACT: The effect of shielding sections of the tissues in the upper region of the abdomen (by using steel blocks of various widths and thicknesses) on the increase in the radiation resistance of animals during a general γ-irradiation in lethal and super-lethal doses was examined in experiments on rats. It was shown that the effect of shielding the abdomen depends on both the width and the thickness of the shield. For γ-radiation in doses of 1000-1650 r, the optimum width of the shield is 2 cm. The minimum thickness of a shield which ensures a high survival rate of the animals varies for various doses of irradiation: 5 cm for a dose of 100 r, 10 cm for a dose of 1500 r. In shielding parts of the upper region of the abdomen of rats by blocks with a width of 2 cm and a thickness of 15 cm, the factor for the decrease of the dose was about 2.4.

Man's penetration into space (and, in particular, prolonged interplanetary flights) can be linked with the appearance of radiation damage which is caused by the injurious biological effect of cosmic radiation, primarily the high-energy protons which are generated during solar flares [1, 3, 4, 5]. Therefore, the great interest which scientists of various countries have in the problem of increasing the radiation resistance of living organisms is completely understandable. /448

Since the time of Jacobson's first experiments [14-16], history has known the method which provides for changing the course of radiation sickness by increasing the radiation resistance of an organism; in particular, the method of shielding various organs or regions of animals' bodies during irradiation. Various authors have established that the most pronounced protective effect (primarily the decrease in the number of fatal results) for a general X-ray irradiation of animals over a wide range of doses is observed when the organs in the abdomen (particularly its anterior region) are shielded [2, 6, 8, 12, 14-19]. Such a location for the shield guarantees preserving parts of the most radiation sensitive organs (the hemopoietic tissue and the intestine) which play an important part in the processes of post-radiation recovery. /449

The authors of this article, together with other collaborators,

have shown that shielding various sections of the body, primarily the anterior region of the abdomen, is an effective method of decreasing the severity of a radiation reaction, not only for the effect of γ-rays, but also for irradiating mice by a pulsed beam of protons with an energy of 120 MeV [7]. It was shown somewhat earlier [9-11] that radiation-protective preparations also maintain their effect when irradiating the animals with protons at energies of 120-660 MeV.

In this article, we are presenting the results of further studies on the effect of shielding the abdomen during the radiation reaction in rats. We paid particular attention to the study of the relationship between the survival rate and the width and (in particular) thickness of the shields for various doses of γ-irradiation. By the width of the shield (the protective block), we mean its vertical dimensions, coinciding with the direction of the sagittal line of the body; by the thickness, we mean the path through which the materials of the protective block for the energy flux pass, and which is directed perpendicular to the sagittal line of the body.

All the experiments were conducted on more than 650 white rats, males and females of no particular strain, weighing 200-250 g. The methods of examining and irradiating the animals while shielding the abdominal region were described in a preceding article [7]. The rats were subjected to a general γ-irradiation from Co^{60} in doses from 100 to 1650-1950 r (13-15 r/min).

For the following reasons, we did not consider it necessary to examine the effect of shielding the abdomen on the radiation reaction of the rats during irradiation in doses which exceeded 1800-2000 r. A large number of experiments have shown that, during irradiation of various large parts of the animals' bodies (head, chest, abdomen) over a definite range of doses, a typical radiation sickness (which often ends in death) develops. The doses of radiation which cause the fatal result vary in relation to the radiation sensitivity of the organs and tissues of the irradiated region of the body, and in relation to their significance during the processes of post-radiation recovery. A detailed examination of the course of radiation damage and the causes for the fatal results after irradiating large parts of the body in rats [13] showed that, even in irradiating the chest (a relatively radiation resistant region) at doses which exceed 2000 r, all the rats died from an acute radiation sickness between the 14th and 26th days after the irradiation. In the case of irradiation of the head, the mass of which is only about 12.5% of the mass of the entire body, all the rats died between the 8th and 17th days in those cases when the dose of the radiation was equal to, or exceeded, 1750 r.

The deaths of the animals after irradiating the head or chest /450
in large doses, despite the protection of the remaining part of the body (and thus the preservation of the principal mass of the most

radiation sensitive organs and tissues which play a determinant part in the processes of post-radiation recovery), can be explained by the irreversible injuries to the cells and tissues of the irradiated areas of the body.

Therefore, shielding almost the entire body (excluding only the head) does not prevent the death of the rats during the first two or three weeks after irradiation in doses which are equal to, or exceed, 1750 r. Obviously, shielding relatively small parts of the anterior region of the abdomen (the location we selected) cannot give a clear positive result for doses of irradiation which are close to, or even exceed, 2000 r.

As we have already said, this experimental study was conducted on rats irradiated by doses which exceeded the minimum absolute lethal dose, equal to about 900 r under our conditions of irradiation. The principal criterion for evaluating the results obtained was selected as the 30 day survival rate of the rats.

It is well known that the effect of the shielding depends on the value for the dose of irradiation, the location of the shield, the area of the shielded surface (the mass of protected tissue), the thickness of the shield, the determining remanent dose beyond the protection, and a number of other factors.

The first experiments were conducted in order to study the problem of the change in the survival rate of the rats for various doses of irradiation, in relation to the width of the shield. In all our experiments, steel shielding blocks were placed perpendicular to the sagittal line of the body (along its lengthwise axis), covering the parts of the anterior region of the abdomen which were directly in front of the umbilical line. Therefore, the width of the blocks determined the value of the area, and thus the value for the mass of protected tissue.

We have already published the first results of the studies on this problem in a previous article [7]. Later, we conducted experiments with the width of the protective blocks decreased to 1 cm, as well as with blocks 2 cm wide for larger doses of radiation (Table 1, Figures 1 and 2). An analysis of Table 1 and Figures 1 and 2 shows that, within the range of irradiation doses from 1000 to 1500 r, the shielding of the abdomen by blocks with a width of 2 to 6 cm, for a constant thickness of 15 cm, produces a very high survival rate of the animals, within the limits from 82 to 97-100 %. Even for a dose of 1650 r, the high survival rate of the rats is preserved, while the numerical differences found in the percentage of the survival rate for shielding the animals with blocks with a width of 3 and 2 cm were statistically unreliable. A decrease in the width of the shield down to 1 cm leads to an intense decrease in the survival rate of the rats for doses of irradiation which exceed 1000 r, while for a dose of 1650 r, all the animals died. Thus, on the basis of the results obtained, we can draw the very

TABLE 1. CHANGE IN THE SURVIVAL RATE OF IRRADIATED RATS, SHIELDING THE ANTERIOR REGION OF THE ABDOMEN BY PROTECTIVE BLOCKS OF VARIOUS WIDTHS AND A THICKNESS OF 15 cm. /451

Dose, r	Width of the Shield, cm	Number of Rats		Survival Rate % ± m	Average Lifespan, in Days, of the Rats which Died, M ± m
		Total	Survivors		
1000	0	95	3	3,2±1,8	7,4±0,3
	6	30	30	100,0	—
	4	30	29	96,7±3,3*	13,0
	3	36	35	97,2±2,8*	7,0
	2	30	25	83,3±6,8*	18,2±4,3
	1	42	38	90,5±4,5*	17,8±1,8
1200	0	12	0	0	4,8±0,4
	4	12	12	100,0	—
	2	24	23	95,8±4,1	24,0
	1	18	6	33,3±11,1	15,4±2,6
1500	0	12	0	0	3,3±0,1
	4	12	12	100,0	—
	3	17	14	82,4±9,2	18,0
	2	17	14	82,4±9,2	16,3
	1	18	2	11,1±7,4	10,9±1,4
1650	0	12	0	0	3,8±0,1
	3	29	24	82,8±7,0	18,2±1,9
	2	30	21	70,0±8,4	14,2±2,1
	1	30	0	0	8,0±0,8
1800	2	18	5	27,8±10,6	10,2±0,9
1950	2	18	0	0	9,2±1,2

*Reliability of the Differences for the Control Irradiation, $p < 0.001$.

definite conclusion that in order to preserve the high survival rate of the rats for doses which exceed the minimum absolute lethal dose by 1.5-2 times, we must consider a width of 2 cm for the shield as most reasonable for the locality we selected, since a further increase of its width does not cause a reliable increase in the survival rate of the animals; a decrease to 1 cm does not guarantee an adequately high survival rate for doses which exceed 1000 r.

In our opinion, the results obtained show sufficiently well that in order to clarify the definite protective effect on the rats (according to the characteristic of the 30-day survival rate) in the range of doses we are examining, there is obviously a certain minimum volume (minimum mass) of protected tissue (primarily in the intestine and the hemopoietic organs), whose normal function must /452
be maintained to ensure recovery from the radiation damage to the organs and tissues.

For the locality we selected, a protective shield with a width of 2 cm immediately guarantees a reliable preservation of the necessary minimum number of vital tissues which have a high regenerative capacity. On the basis of the calculated data presented in our previous study [7], we can easily determine that for a shield with a width of 2 cm, the mass of protected tissues is about 10-12% of the entire mass of a rat's body, i.e. about 25 g (for a total weight of 200-250 g). At the same time, if the mass of protected tissues is only 5-6% of the entire mass of the body, which is the case for a shield with a width of 1 cm, this quantity is insufficient for guaranteeing a high survival rate of the rats after γ-irradiation in doses which exceed 1000 r.

Our conclusion regarding the existence of a minimum volume (mass) of the intestine and hemopoietic tissue which is necessary for obtaining a reliable protective effect in shielding the abdomen in rats conforms in this respect to the data of Mezen et al. [6]. /453

The following stage of the study involved an experimental examination of the effect on the survival rate of the rats produced by shielding the abdomen with blocks of varying thicknesses and the

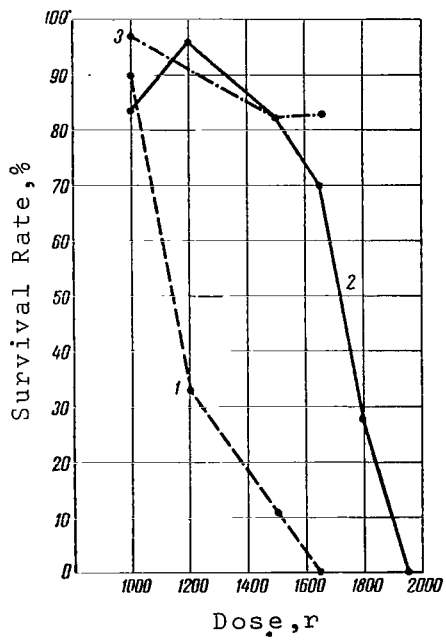

Fig. 1. Survival Rate of the Rats, Shielding the Abdomen by Blocks with a Thickness of 15 cm Versus the Dose of Irradiation, for Various Widths of the Blocks: (1) 1 cm; (2) 2 cm; (3) 3 cm.

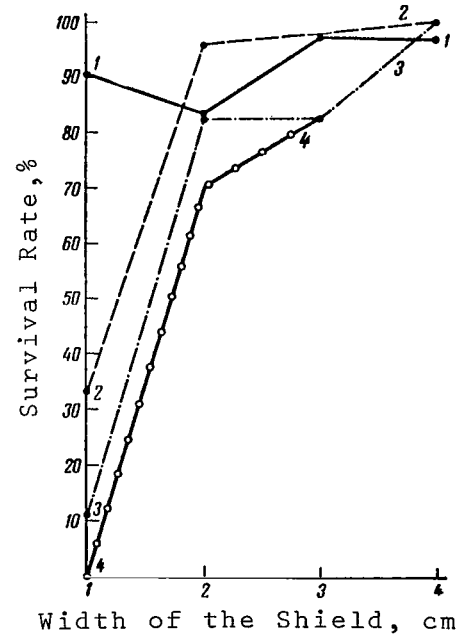

Fig. 2. Survival Rate of the Irradiated Rats Versus the Width of the Shield for Various Doses of Gamma Radiation: (1) 1000 r; (2) 1200 r; (3) 1500 r; (4) 1650 r. The Thickness of the Shield is 15 cm.

same width. The examinations were conducted with blocks 3, 5, 10, and 15 cm thick, widths of 1 and 2 cm, and an irradiation dose of 1000 r, as well as with blocks 5, 10, and 15 cm thick, 2 cm wide, and a dose of 1500 r (Table 2, Fig. 3).

For a dose of radiation of 1000 r, the shielding of the abdomen by a block 1 cm wide and 3 cm thick, although it led to a small increase in the survival rate of the rats, nevertheless showed a statistically unreliable increase, in comparison with the control for irradiation. An increase in the thickness of the shield up to 5 and 10 cm increased the survival rate of the rats up to a reliable level, in comparison with the control group (21-29% deaths, 3.2% in the control). Only for a thickness of 15 cm was there a high (about 90%) survival rate of the rats which were irradiated by a dose of 1000 r.

TABLE 2. CHANGE IN THE SURVIVAL RATE OF IRRADIATED RATS WITH SHIELDING OF THE ANTERIOR REGION OF THE ABDOMEN BY PROTECTIVE BLOCKS OF VARYING THICKNESSES

Dose of Irradiation r	Dim. of the Shield, cm		No. of Rats		Survival Rate		Average Life time in Days, for the Rats which Died, $M \pm m$
	Width	Thickness	Irradiated	Survived	% $\pm$ m	Rel. of the Diff. in the Control	
1000	Without Shield		95	3	3,2±1,8		7,4±0,3
	1	3	24	2	8,3±5,6		9,3±1,3
		5	24	5	20,8±8,3	$p < 0,05$	11,3±1,2
		10	24	7	29,2±9,3	$p < 0,01$	10,6±1,0
		15	42	38	90,5±4,5	$p < 0,001$	17,8±1,8
	2	3	48	7	14,6±5,1	$p < 0,05$	12,9±0,9
		5	42	37	88,1±5,0	$p < 0,001$	14,0±2,1
		10	42	39	92,9±4,0	$p < 0,001$	17,7 (3)
		15	30	25	83,3±6,8	$p < 0,001$	18,2±4,3
1500	2	5	24	2	8,3±5,6		8,5±1,0
		10	18	9	50,0±11,8		10,6±1,8
		15	17	14	82,4±9,2		16,3 (3)

With the same dose of irradiation, but with a shield-width increased by a factor of 2, all the experimental variations of thicknesses for the protection resulted in a reliable (in comparison with the control for irradiation) increase in the survival rate of the animals. It is true that, for a shield-thickness of 3 cm, the percentage of survivals was still small (14.5%), but even for a thickness of 5 cm, the survival rate reached a very high level. A further increase in the thickness of the protection to 10 and 15 cm had no substantial effect on the survival rate. Certain numerical differences in the percentage of survivals for block thicknesses of 5, 10, and 15 cm are statistically unreliable. /45

As we have already shown, for a dose of irradiation of 1500 r, shielding of the abdomen by blocks with a width of 1 cm, even at the maximum thickness we examined (15 cm), gave a not-too-convincing result - the survival rate of the rats was about 11% in all. Therefore, the study of the effect of the thickness of the protection on the survival rate of the rats during irradiation by a dose of 1500

r was conducted only for a shield width of 2 cm. For a shield thickness of 5 cm, the survival rate was very low (8%); even for a /455 thickness of 10 cm, it was 50% and for a thickness of 15 cm, it reached a very high level, almost 82.5%. In other words, the shielding

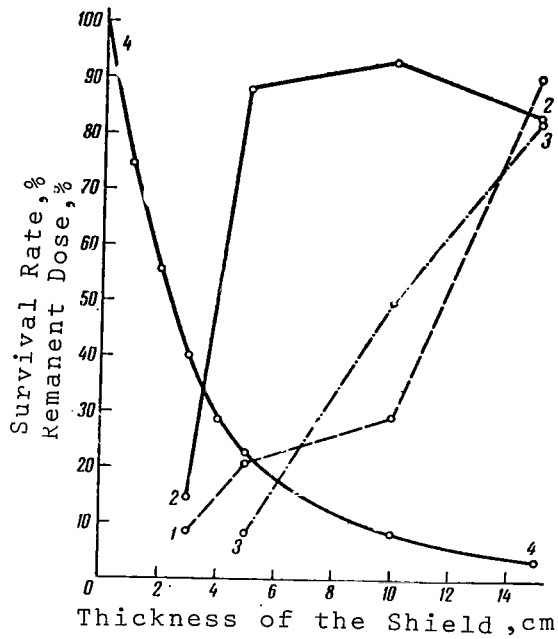

Fig. 3. Survival Rate of Irradiated Rats Versus Thickness of the Shield (Remanent Dose beyond the Shield) for Various Values of Shield-Width and the Dose of γ-Radiation. (1) Width of 1 cm, Dose of 1000 r; (2) Width of 2 cm, Dose of 1000 r; (3) Width of 2 cm, Dose of 1500 r; (4) Remanent Dose Beyond the Shield.

of the abdomen by a block with a width of 2 cm and a thickness of 15 cm during general γ-irradiation by a dose of 1500 r guaranteed practically the same survival rate as for a dose of 1000 r, for a shield of the same width and thickness from 5 to 15 cm.

It is well known that the thickness of a shield determines the degree of the weakening of the radiation dose by the protective materials, and thus also determines the value for the so-called remanent dose, which reaches the shielded tissue and causes its irradiation.

For a quantitative evaluation of the radiation dose for those parts of the body beyond the shield, we measured the remanent dose rate after the flux of γ-rays passed through a steel shield with dimensions of 2 x 40 cm, and a thickness from 1 to 15 cm. With such a "narrow" geometry for the protection, the supplementary contribution to the dose of irradiation of the animal was caused mainly by the diffusion of the γ-radiation in the layer of air

between the irradiator and the irradiated object. The use of shields with large widths leads to an increase in the number of elements with large atomic numbers between the source and the irradiated object, and this then increases the relative contribution to the radiation dose because of the diffusion of the gamma rays in the protective materials. In relation to this, we made measurements for the dose beyond a shield with dimensions of 10 x 40 cm, and with a thickness from 1 to 5 cm ("wide" geometry for protection) (Table 3).

The dosimetry of the gamma radiation was made by generally accepted methods, with the aid of capacitor direct-indicating dosimeters (Type DKP-50).

TABLE 3. VALUE FOR THE REMANENT DOSE BEYOND STEEL SHIELDS OF VARIOUS THICKNESSES, FOR "NARROW" AND "WIDE" GEOMETRY OF PROTECTION

Thickness of Shield cm	No. of Measurements	"Narrow Protection" Dose Rate, r/min, $M \pm m$	"Narrow Protection" Remanent Dose Rate, %	"Wide" Protection Dose Rate, r/min, $M \pm m$	"Wide" Protection Remanent Dose, Rate %
0	10	13,7±0,2	100	13,6±0,27	100
1	10	10,2±0,18	74,5	11,8±0,24	86,8
2	10	7,6±0,12	55,5	9,0±0,15	66,3
3	10	5,5±0,13	40,0	7,1±0,14	52,3
4	10	3,9±0,09	28,4	5,37±0,12	39,4
5	10	3,1±0,06	22,9	4,0±0,1	29,4
10	6	1,1±0,07	8,1	—	—
15	12	0,48±0,06	3,5	—	—

TABLE 4. REMANENT DOSE BEYOND THE SHIELD, AND SURVIVAL RATE OF THE /456 IRRADIATED RATS, WITH SHIELDING OF THE ANTERIOR REGION OF THE ABDOMEN

Dose, r	Dimensions of Shield, cm: Width	Dimensions of Shield, cm: Thickness	Survival Rate, % ± m	Remanent Dose Beyond the Shield: % of the Dose of Irradiation	Remanent Dose Beyond the Shield: Approximate Value, r
1000	1	3	8,3±5,6	40,0	400,0
		5	20,8±8,3	22,9	230,0
		10	29,2±9,3	8,1	80,0
		15	90,5±4,5	3,5	35,0
	2	3	14,6±5,1	40,0	400,0
		5	88,1±5,0	22,9	230,0
		10	92,9±4,0	8,1	80,0
		15	83,3±6,8	3,5	35,0
1500	2	5	8,3±5,6	22,9	350,0
		10	50,0±11,8	8,1	120,0
		15	82,4±9,2	3,5	50,0—55,0

As we can see from Table 3, an increase in the thickness of the shield produces a regular decrease of the remanent dose, while in the case of a "wide" geometry for protection, the value of the dose was 10% higher on the average under our conditions for irradiation than in the case of a "narrow" geometry for the same thickness.

A comparison of the results of the biological experiments studying the effect of shielding the abdomen with blocks of various thicknesses on the survival rate of the irradiated rats and the data on the physical measurements of the remanent dose beyond the same blocks is of definite interest. This comparison allows certain preliminary conclusions to be drawn.

For the principal shield width which we selected (2 cm), there is an increase in the survival rates of the animals (by no less than 50%) for the range of doses from 1000 to 1500 r, not only in those cases when the protective shield absorbs almost all the flux of γ-rays (as observed for a thickness of protection of 15 cm), but also when the shielded parts of the body receive relatively large doses of radiation: up to 100-120 r for a dose of 1500 r (shield thickness of 10 cm), and up to 230-250 r for a dose of 1000 r (thickness of 5 cm) (Table 4).

The varying value for the maximum doses of radiation to the shielded parts of the tissues (approximately 120 to 250 r), at which these tissues still preserve their ability to show a protective effect, can be explained by the difference in the value of the radiation dose and therefore by the degree of severity of the damage /457 to the non-protected tissues and organs, which make up about 90% of the mass of a mouse's body.

It is well known that for mice, the greatest protective effect is noted during shielding of the spleen; for rats, this is observed during shielding of parts of the bone marrow and the small intestine. It has been shown [17, 18] that for a general X-ray irradiation of mice in a dose of 1025 r, the survival rate in the control groups averaged about 1%, while in the groups where the spleen was completely protected, 77% of the mice survived. In some groups of mice, a protection of the spleen by lead was temporarily eliminated, so that the spleen was subjected to irradiation in doses from 50-600 r, while the entire body was subjected to irradiation at a dose of 1025 r. It was established that for a dose of irradiation of the spleen of 200 r, 75% of the mice survived, while for doses of 400, 500, and 600 r, 59, 50 and 34% of the mice survived. The authors consider that the ability of the spleen tissue to show a protective effect is still partially preserved, or is rapidly recovered, so that the survival rate of the mice is increased even at such high doses of irradiation as 600 r for the spleen and 1025 r over the entire body of the animal.

Turning again to the data which are listed in Table 4, we see that they still are a convincing indication of the significance of

the value of the mass of the animal tissue which is shielded during the irradiation in finding a definite protective effect. With irradiation of the rats by a dose of 1000 r while shielding the abdomen by a block with a width of 1 cm, when the mass of shielded tissue is decreased by a factor of 2 in comparison with the mass protected by a block with a width of 2 cm, the maximum value for the radiation dose of the protected tissues at which there is observed a high survival rate of the irradiated rats is only several tens of roentgens. In any case, for a radiation dose for the protected tissues equal to 80 r and more, the survival rate of the animals during shielding by a block of this width does not exceed 20-30%, while the survival rate in the control group is about 3%. At the same time, as we already saw, during shielding of the abdominal organs with a block of 2 cm in width, up to 50% of the irradiated rats survived, even with an increase of the dose of general irradiation by 1.5 times (up to 1500 r), in those cases when the dose beyond the shield reached 120 r.

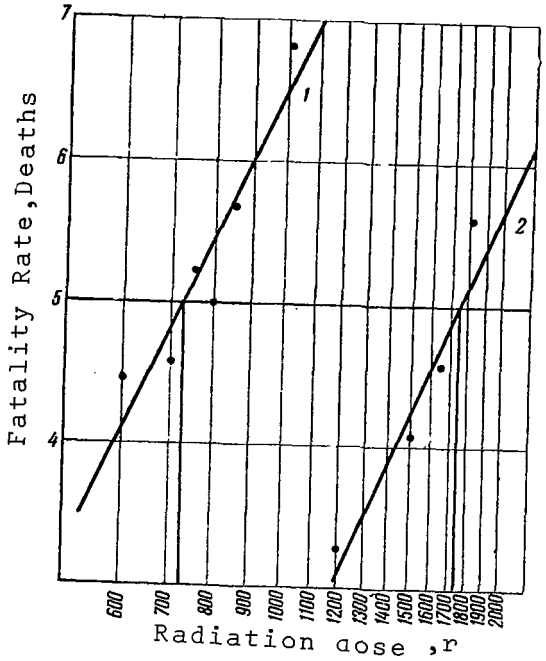

Fig. 4. Death-Lines for the Fatality Rate of Rats for Various Doses of γ-Irradiation. (1) Control, for Irradiation; (2) Shielding the Abdomen with Blocks 2 cm Wide and 15 cm Thick.

Thus, a reliable increase in the survival rate of the irradiated animals, linked with an increase in their radiation resistance, is observed during shielding of parts of the abdominal cavity, not only under the conditions of a complete protection of the organs and tissues of these parts of the abdomen from the direct effect of ionizing radiation, but also in those cases when the shielded organs and tissues still undergo the direct effect of radiation in doses which exceed a certain value, differing for different doses of general irradiation. For example, for a dose of general γ-radiation for rats equal to 1000 r, the high protective effect of shielding the abdomen (according to the survival rate for 30 days) is preserved even in that case when the dose for /458 for irradiating the shielded sections of the abdominal cavity is about 25% of the dose for general irradiation.

The experiments which we conducted again showed that shielding parts of the body during general irradiation of animals can be used

as a method for increasing their radiation resistance. For lethal doses of radiation, the shielding of certain parts of the body, in particular the anterior region of the abdomen in rats, with definite measurements for the width and thickness of the protective shield, leads primarily to a substantial increase in the survival rate of the animals.

A question could arise: does the shielding method have any advantages over other methods for increasing the radiation resistance of animals, particularly in comparison with the method of pharmacochemical protection? In our opinion, both methods have their advantages and disadvantages, a detailed examination of which is not included in the scope of this study.

Nevertheless, we would like to emphasize that the shielding of /459
various parts of the body during general irradiation of animals ensures achieving a high survival rate for a wider range of doses than even for the most effective radiation protectors. In analyzing the results of our experiments by the death method (Fig. 4), for a general γ-irradiation of rats, $LD_{50/30}$ = 725 r, and for rats whose anterior region of the abdomen is shielded (by a block with a width of 2 cm and a thickness of 15 cm), $LD_{50/30}$ = 1730 r. Thus, the shift in the $LD_{50/30}$ in this case was about 1000 r, while the factor for the decrease of the dose was about 2.4. At the same time, the factor for the decrease of the dose is roughly equal to 1.5-1.7 for most effective radiation protectors, and sometimes it is less.

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CRITERIA FOR RADIATION SAFETY DURING PROLONGED SPACE FLIGHTS

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ABSTRACT: The criteria for determining the radiation danger of space flights are examined in the article. It was shown that the selection of the criteria should be based on a consideration of the spectral composition and the type of cosmic radiation, as well as the degree of uniformity for the distribution of the absorbed dose. In planning protection from cosmic radiation, it is recommended that specially-analyzed norms for the possibility of irradiating the astronauts during the flight be used.

The advances in the conquest of space have made the hope of /460
prolonged trips in manned space flights very feasible. In relation to the fact that during prolonged space flights the doses of ionizing radiation on humans and elements of the biological complex become dangerous, the problem of protection from cosmic radiation acquires importance.

In working with sources of ionizing radiation under terrestrial conditions, the solution to the problem of protection was based on a large number of radiobiological and physical examinations. Naturally, similar examinations are also necessary for guaranteeing radiation safety during space flights. The most important tasks of these examinations include analyzing the principles for guaranteeing radiation safety and establishing the criteria which determine the security of space flights.

PRINCIPLES FOR GUARANTEEING RADIATION SAFETY DURING SPACE FLIGHTS

On the basis of experiments with atomic electric power stations and the atomic ice-breaker "Lenin", we can state that for a reliable guarantee of radiation safety for the crew, it is necessary to plan a special system for radiation safety. This system is a combination of physical, technical, medical and hygienic means and methods intended for providing safe conditions for the occupational activity of the crew. The system of radiation safety includes the following: protection from penetrating radiation, a system of dosimetric control, medical and hygienic methods including means for pharmacochemical protection, etc.

The necessity of producing a system of radiation safety is maintained without exception under the conditions of a space flight.

Because of the rigid weight and bulk requirements now imposed on the habitable compartments of spacecraft, it is of practical necessity to produce a general protection from radiation which guarantees a decrease in the radiation effects down to the level of the maximum permissible doses of occupational exposure acceptable under terrestrial conditions.

In relation to this, the solution to the problem of protecting /461 an astronaut and the life-reservation systems must obviously be found in a combined use of general protection of the habitable compartments, radiation shelters, local protection of the astronauts, and pharmacochemical prophylactic means.

On board the craft, there should be a system of dosimetric control which is intended for determining the radiation effects on the members of the crew, and biological systems for life preservation, as well as for signaling and informing the crew of a worsening of the radiation situation. The task of dosimetric control on board a spacecraft is rather complex for a number of reasons. This is mainly related to the necessity of considering the spatial distribution of the absorbed dose in the body of the astronaut, and the complex variety and composition of the radiation acting on the spacecraft.

Under the conditions of space flight, it is possible that there could be an unforeseen significant worsening of the radiation situation, for example, during the appearance of gigantic chromospheric flares. In relation to the definite probability of such occurrences, the spacecraft should be supplied with means for pharmacochemical protection as well as for therapy after radiation damage [4].

In guaranteeing radiation safety of space flights, great significance is given to a terrestrial station for radiation safety, the principal task of which is to generalize the information on the radiation situation during the period preceding the flight and during it, to predict the possible radiation effect on the basis of the information transmitted from a station which observes the solar activity (and transmitted from on board the craft), and to obtain operative solutions for guaranteeing the radiation safety of the astronauts.

Thus, the system of radiation safety should consist of the following basic elements:

(1) Radiation protection which includes a general protection of the compartments, a radiation shelter, and local protection.

(2) A radiation dosimeter which includes an on-board dosimeter, a separate dose-regulator, signal devices, and notification.

(3) Medical and hygienic means, including methods for pharmacochemical prophylaxis and radiation-damage therapeutics.

(4) A terrestrial station for radiation safety.

PHYSICAL BASIS FOR THE CRITERIA OF RADIATION SAFETY DURING SPACE FLIGHTS

The selection of the criteria for radiation safety is the principal problem in planning protection from cosmic radiation. In a number of studies [22, 23, 26], such a criterion was found in the local absorbed dose, i.e., the radiation energy absorbed in 1 g of /462 tissue.

This criterion cannot be recognized as the correct one, for many reasons. First of all, during the process of the interaction between the radiation and the substance of the biological tissue, there is a definite spatial distribution of the absorbed dose within the limits of the human body. The spatial distribution depends on the spectral-angular distribution of the radiation striking the body; in relation to this, a correspondence between the value for the local absorbed dose and the dose absorbed in a gram of body tissue can be found only in certain particular cases. Secondly, although a local absorbed dose can represent the radiation effect on microscopic objects, it cannot characterize the effect on large biological objects in the same way, because of the inter-relationships between damaged organs and tissues, their relative radiation sensitivity, etc.

In our opinion, the criterion for radiation safety should be selected by considering the spectral composition and the type of incident radiation acting on the human body. If the penetrability of the radiation is great, and there is a relatively small decrease in the doses within the limits of the human body, then we can use the mid-tissular absorbed dose as such a criterion. If the penetrability of the radiation is such that the absorbed doses differ greatly at various points in the human body, then the value of the mid-tissular dose, averaged over the entire body, does not give a sufficient representation of the degree of radiation danger; in this case, it is necessary to use the data on the spatial distribution of the absorbed dose in the body.

When the cosmic radiations penetrate the protective substance and the tissues, various secondary particles (protons, mesons, emission nuclei, etc.) are formed and take part in the formation of the biological dose in the body. The biological effect of each type of ionizing radiation depends on the value of the ionization losses, the values of the doses, and the times of the irradiations. At present, the relationship between the relative biological effectiveness (RBE) and the chronic conditions of irradiation are generally used. Obviously, this leads to a certain overestimation of the values for the doses. In order to obtain more accurate data, we must determine the biological effectiveness of the corresponding types of radiation under conditions which best approximate those of a space flight.

Let us examine further the principal sources of radiation in space.

The galactic cosmic radiation (GCR) consists mainly of protons, α-particles, and light nuclei. The integral flux of the GCR is 1.8-4.0 particles /cm^2·sec, in relation to the solar activity [1, 2, 5, 12, 27]. The angular distribution of the GCR is generally considered isotropic. The spectrum for all the components of the GCR with an energy of more than 1 BeV/nucleon can be represented as a power function with an exponent from 2.0 to 2.5. /463

As a result of the high penetrability of the GCR, the spatial distribution of the dose over the body is almost homogeneous obviously. However, in relation to the high linear ionization losses of the heavy ions included in the GCR, the biological effectiveness of this radiation has great significance. According to our calculations [8], the total effect of the GCR when there is no protection is equal to 22 mrad/day, or 130 mrem/day. In order to orient the evaluation of the contribution to the dose from the secondary radiation arising in the protection and the body of the astronaut during the effect of GCR, we can use the data on the altitude dependence of the ionization produced by the GCR in the atmosphere. This evaluation shows that the contribution of the secondary radiation is 50-100%. Considering this dose, the GCR in interplanetary space can reach 200-250 mrem/day [8]. Obviously, the GCR can present serious danger to the astronauts in the case of prolonged flights.

In the immediate proximity of the Earth, the GCR dose is much lower because of the shielding effect of the Earth itself and its magnetic field. Thus, for an orbit located at an altitude of 200-600 km, with an angle of inclination toward the plane of the equator of 65°, the GCR dose including the secondary radiation is 8-10 mrad/day. These results conform well with the data from direct measurements during the flight of the "Vostok" craft [10,11].

The inner radiation belt is located within the area limited by the magnetic line of force which intersects the Earth's surface at a geomagnetic latitude of 45°. In the Western Hemisphere, this region begins at an altitude of 500-600 km (1500 km in the Eastern Hemisphere). The belt extends up to an altitude of about 10,000 km. The maximum intensity is observed at an altitude of about 3600 km from the surface of the Earth (the first maximum); the second maximum is observed at an altitude of about 7000-8000 km from the Earth's surface. The principal component of the radiation in this belt is high-energy protons [24, 25, 28].

The omnidirectional intensity of the flux for protons with an energy of more than 40 MeV is $2 \cdot 10^4$ at the first maximum, and about $5 \cdot 10^3$ particles/cm^2·sec at the second maximum. The spectrum for the protons of the zone can be represented by a power function with an exponent from 1.4 to 1.8, in relation to the segment of the spectrum of the protons [24, 25, 28].

The spatial distribution of doses, calculated for a spherical phantom with a diameter of 50 cm, is shown in Figure 1 in relation to various thicknesses of an aluminum shield [8]. The decrease of the dose in this case is such that the use of the mid-tissular dose is valid, even for shields with thicknesses greater than 1 g/cm^2. /464
The values of the mid-tissular doses of the protons for various circular orbits beyond an aluminum shield of 1 g/cm^2 are shown in Table 1 [8].

The outer radiation belt consists mainly of electron fluxes. The outer zone is located in the area which is 10,000-50,000 km over the Equator,and which drops down to 300 km at latitudes of 55-70°. The maximum intensity of the outer belt is found at a distance of 15,000-20,000 km from the Earth. In this belt, the flux of electrons with energies higher than 40 KeV is about 10^8 particles/cm^2·sec. The spectrum of the electrons at the center of the zone can be represented by a power function with an exponent of 2 ± 0.5. The angular distribution of the electrons in this zone is generally considered to be isotropic [2,15].

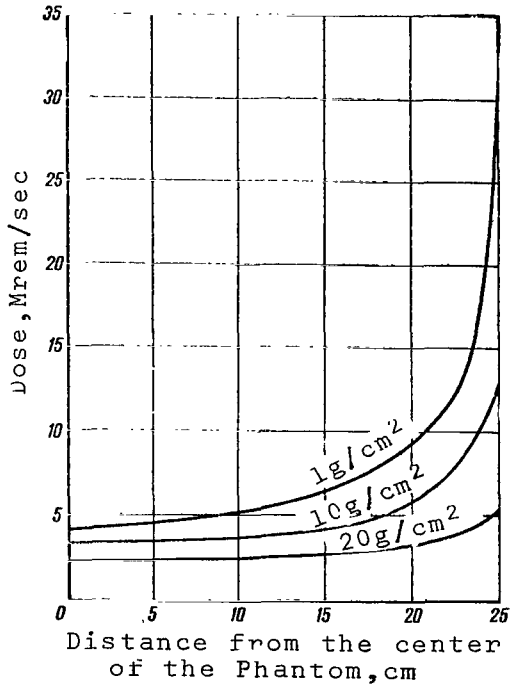

Fig. 1. Spatial Distribution of the Dose of Protons Absorbed by Tissue in the Inner Radiation Belt, Using a Spherical Phantom (r = 25 cm), for Various Thicknesses of an Aluminum Shield.

The electrons of the outer belt have little penetrability, and affect mainly the integuments. At the center of the zone, for a shield of a light substance with 1 g/cm^2, the dose rate at the surface of the body is 40 rad/day (calculated according to the /465
method presented in article [18]). In this case, the mid-tissular dose caused by bremsstrahlung (calculated according to the method presented in the article [16] is about 1 rad/day.

TABLE 1. MID-TISSULAR DOSES OF THE PROTONS (IN REM/DAY)(SPHERICAL PHANTOM) (CALCULATED DATA)

Height above the surface of the Earth, km.	Angle of Inclination to the Plane of the Orbit			
	0°	45°	65°	90°
300	<0,05	<0,05	<0,05	<0,05
500	0,16	0,16	0,16	0,16
1000	2,0	0,9	0,65	0,58
2500—3500	110	26	20	18
7500	2,6	3,4	2,6	2,4

The artificial radiation belt of the Earth, formed as a result of a number of high-altitude nuclear explosions, consits of electrons with energies up to 7 MeV. The spatial distribution and fluxes of electrons change greatly in time. The most stable part (with a disentegration constant of 1-3 years) is located at a distance of 1200-4500 km above the Equator. At the center of the artificial belt, at an altitude of 1800-2300 km, the omnidirectional intensity of the electrons whose energies are greater than 0.5 MeV was $(5\text{-}10)\cdot10^8$ particles/cm^2 sec at the end of 1962 [25].

Table 2 shows the values for the surface doses caused by the electrons of the artificial belt, which we calculated according to the method in [18] for a shield of 1 g/cm^2.

TABLE 2. SURFACE DOSES OF ELECTRONS (IN RAD/DAY) OF THE ARTIFICIAL BELT FOR THE YEAR 1962 (CALCULATED DATA)

Height above the surface of the Earth km	Angle of Inclination to the Plane of Orbit			
	0°	45°	65°	90°
1000	$3\cdot10^3$	$6\cdot10^2$	$4{,}5\cdot10^2$	$4{,}2\cdot10^2$
1800—2300	$2\cdot10^5$	$2{,}4\cdot10^4$	$1{,}9\cdot10^4$	$1{,}7\cdot10^4$
3000	$4{,}4\cdot10^4$	$8\cdot10^3$	$6{,}5\cdot10^3$	$5{,}9\cdot10^3$
8000	$2{,}8\cdot10^3$	$7\cdot10^2$	$5{,}5\cdot10^2$	$5\cdot10^2$

The dose from the bremsstrahlung, for protection with a thickness of 1 g/cm^2, is much less than the doses from the electrons. The spatial distribution of the dose from the bremsstrahlung of the electrons at the center of the artificial belt, calculated for a spherical phantom with a diameter of 50 cm, is shown in Figure 2. /466

For the electrons of the radiation belts, the decrease of the dose by the thickness of the body is very great. Therefore, in calculating the radiation effect as a criterion of the radiation safety, it is more correct to use the maximum (surface) dose.

The solar corpuscular radiation (SCR) arises during chromospheric flares on the Sun. The frequency of the appearance of solar flares is related to the activity of the Sun. During a period of the maximum solar activity, about 5-13 flares of low intensity occur in a year; during a period for the minimum solar activity, the frequency of flares decreases. Solar flares which are accompanied by high-intensity radiation occur 1-2 times in 5 years. During this period of minimum solar activity (1964-1966), solar flares are very infrequent, and their frequency will increase during the following period (1969-1970).

The corpuscular radiation of the solar flares consists mainly

of protons and α-particles. With protection by a thickness greater than 3-5 g/cm^2, the contribution from the α-particles is small. The spectrum of the protons of the solar flares contains particles with energies from several MeV to tens of BeV. As a result of this, there are significant decreases of the doses at various points of the body when the thickness of the protection is low (Fig. 3). With an increase in the thickness of the protection, there is filtration of the high-energy protons and the decrease of the dose in the body is subdued.

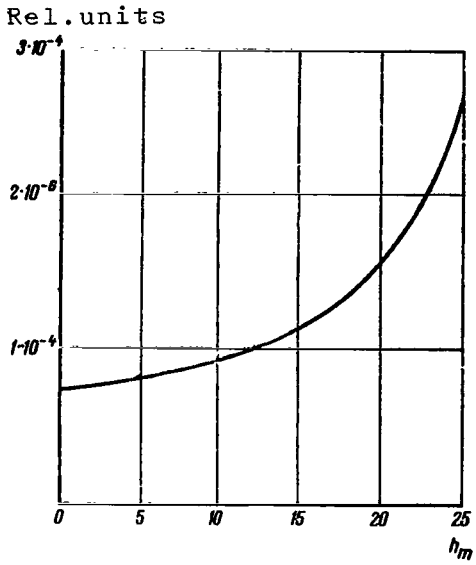

Fig. 2. Spatial Distribution of the Dose Absorbed by the Tissues from Bremsstrahlung of Electrons, at the Center of the Artificial Belt.

Table 3 shows the values for the doses at a point target and in a model of a spherical phantom, for aluminum shielding with 1 g/cm^2 [9].

TABLE 3. DOSES OF RADIATION FOR CERTAIN SOLAR FLARES (IN RAD/FLARE) /467

Date	Point Target	Spherical Phantom
Feb.23,1956	560	82
Nov.12,1960	2200	90
May 10,1959	8600	270

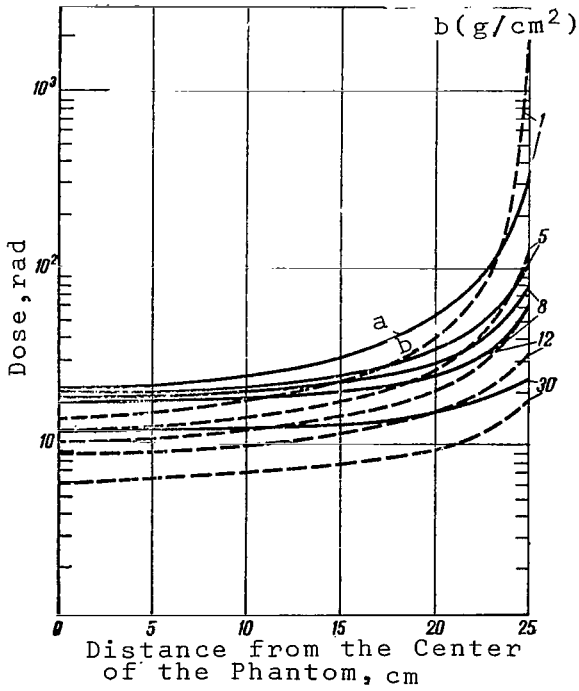

Fig. 3. Spatial Distribution of the Dose Absorbed by the Tissues, Using a Spherical Phantom (r = 25 cm), for Various Thicknesses of an Aluminum Shield (b).
(a) Flare on February 23, 1956;
(b) Flare on November 12, 1960.

RADIOBIOLOGICAL STUDIES

Special radiobiological studies have great significance in solving the problem of radiation safety in space flights. /468

The principal task of these studies is to obtain information on the relationship between the damaging effect of the cosmic radiation and the type and energy of radiations, the dose rate, and the spatial distribution of the absorbed dose, the damage to the critical organs, and the presence of reparative and compensatory processes in an organism, for repeated and chronic irradiations. The solution to these problems indicates the permissible levels of irradiation for the crew, and allows working out recommendations in the case of an excess of irradiation. Moreover, they are also a prerequisite for conducting studies to find effective means of treatment and prophylaxis for radiation damage caused by the effect of cosmic rays.

THE RBE OF COSMIC RADIATION

At the present, it still does not seem possible to make a complete generalization in relation to the RBE of all the components of cosmic radiation. This is primarily due to the fact that there are significant technical difficulties in obtaining (under terrestrial conditions) certain types of radiation whose energy is comparable to cosmic radiation. These difficulties in determining the RBE of cosmic radiation are also found in the imperfection of tissular dosimetry, which does not (as a rule) give precise information on the absorbed energy so that the corresponding comparisons can be made. Moreover, the experimenters can become involved in many complex problems in evaluating a number of factors which can greatly affect the biological effect. In particular, the RBE can very in relation to the biological objective selected, the types of animals and plants, and the index being studied (radiation damages to the skin, hemopoietic organs, crystalline lens, nervous system, etc.). Particularly substantial differences are found in evaluating the genetic changes. Under otherwise equal conditions, the RBE can vary depending on whether the effects of a single acute effect are being examined, or whether an evaluation is being made for the appearances of chronic or fractionated effects of radiation.

Studies in determining the radiation damage caused by the effect of protons, and in clarifying their relative biological effectiveness, have been going on in the U.S.S.R. for a number of years [6, 13, 17, 21].

Experimental animals (dogs, rats, and mice) were subjected to irradiation by protons generated in a synchrocyclotron at the Laboratory of Nuclear Problems, Joint Institute for Nuclear Research, Dubna. The RBE coefficients of the protons were determined on the basis of a comparison of the survival rates, as well as the severity of the radiation damage caused by the effect of protons /469

on the one hand and by x-rays or γ-rays on the other. In the experiments on the dogs, the effects of the irradiation were determined by the animals' general condition, the morphological and biochemical composition of the peripheral blood and bone marrow, the state of the cardiovascular system, the immunological reactivity, and morphological and histological examinations.

In experiments on dogs [6,17], it was shown that irradiation of the animals by protons of 126, 240, and 510 MeV led to the development of radiation damage which is generally characteristic of acute radiation sickness caused by the effect of "standard" types of radiation. However, despite the well-known similarity and typicality of the damages after irradiation by protons, there were also certain differences. First of all, we should note that there were more intense destructive changes in the vessels of all the animals. As a result of this, hemorrhagic symptons were noted more clearly. The hemorrhages were significant during the immediate periods, and they appeared in large numbers. An unusual location of these hemorrhages was also characteristic. Another difference was the more intense suppression of medullary hemopoiesis, particularly in the erythropoeitic section.

On the basis of a similar clinical characteristic for the radiation damage, and by comparing the fatal effects, the RBE of the protons was determined. The RBE coefficient for a repeated irradiation of dogs by protons of 510 and 126 MeV was equal to one unit. For a single irradiation, it increased up to 1.2 for protons of 510 MeV and decreased to 1.0 for protons of 240 and 126 MeV (Table 4).

In parallel studies conducted on smaller laboratory animals, it was shown that the biological effectiveness of protons of 510, 210, and 126 MeV, in relation to rats and mice, was somewhat less than that for γ-rays from Co^{60}.

All the above, in relation to the problem of the RBE, helped mainly in establishing the biological effectiveness of cosmic radiation for animals and human beings. However, in relation to the proposal that higher and lower plants be stocked on board the spacecraft, as a means of guaranteeing the safety of the crew during prolonged flights, the problems of establishing the norms for irradiation of plants and determining the RBE of the cosmic radiation relative to them, also acquire primary importance.

It is very unfortunate that the RBE of various types of ionizing radiation in relation to plants is still not considered as important as that in relation to animals. The data in the literature mainly encompass problems related to a determination of the RBE on the basis of the genetic effects, primarily in comparing /470
the effects of neutrons and x-rays or γ-rays. There are practically no studies on the RBE of protons in relation to plants.

TABLE 4. RBE COEFFICIENTS FOR PROTONS WITH AN ENERGY OF 126-510 MeV

Biological Object (Type of Animal)	Nature of Irradiation	Energy of Protons, MeV	RBE Coefficient
Dogs	Repeated 19 times in 5 weeks	510	1.0
"	same	126	1.0
Rats	Repeated 20 times in 5 weeks	510	0.8
Dogs	Single	510	1.2
"	same	240	1.0
"	"	126	1.0
Rats	"	510	0.75
"	"	240	0.73
"	"	126	0.80
Mice	"	240	0.65
"	"	126	0.55

The examinations we conducted to determine the RBE coefficients of protons with energies of 126 and 660 MeV in relation to seeds of Chinese cabbage showed that on the basis of the somatic effects during radiation over a large range of doses (from 500 to 500,000 rad), the RBE value is 1.6-2.0. Different results were obtained in determining the RBE on the basis of a calculation for the chromosome aberrations in the primary rootlets of the cabbage seeds. For irradiation in doses up to 10,000 rad, the RBE coefficient was equal to 1.0; then it gradually began to increase, reaching 2.0 to 2.2 for protons with energies of 660 and 126 MeV at doses of 100,000 and 21,000 rad, respectively. It is interesting to note that the RBE of protons with an energy of 660 MeV, at a radiation dose for the seeds of 21,000 rad, was equal to 1.2, i.e., the protons with an energy of 126 MeV were more effective than the former by 1.9 times. The results obtained indicate that protons with these energies were more effective in relation to the seeds than in relation to mammals.

Therefore, an analysis of the available data on the RBE of various types of cosmic radiation shows the necessity for conducting similar types of studies, particularly with protons of various energies and with multiply-charged ions, since this information is essential for evaluating the radiation safety for the links of /471
higher and lower plants in the closed system of substances aboard future interplanetary craft.

CRITICAL ORGANS

In addition to establishing the RBE of the cosmic radiations, a very important part of radiobiological research should involve an examination of the biological effects produced by varying the

spatial distributions of absorbed energy. The high energy spectrum of the cosmic radiation causes varying distributions of the absorbed dose with depth. This then obliges us to evaluate the radiation danger on the basis of the injury to the so-called "critical organs", in relation to the fact that this is now done when radioactive substances are found within an organism.

We should note that the particular conditions which are characteristic of space flight call for adding certain new concepts to the existing ones for the "critical organs". Obviously, it is necessary to consider the vestibular analyzer as a critical organ, in addition to the other generally-accepted critical organs (bone marrow, gonads, crystalline lens, skin, etc.). This is dictated primarily by the circumstance that, under the conditions of a space flight, the analyzer is subjected to the effect of adequate stimuli (rectilinear and angular accelerations, Coriolis forces). Moreover, it functions under the conditions of disruption of the interactions of the analyzer systems. In this case, we have in mind the change in the impulses from the otolith apparatus, the proprioreceptors, and other sensitive systems under the conditions of partial or complete weightlessness. A disorder in the activity of the vestibular analyzer can be the cause of an organism's stress reactions, as well as other vestibulo-vegetative and somatic disorders.

As our studies (conducted on 600 rabbits) showed, the statokinetic analyzer was very sensitive to ionizing radiation [7, 14, 19, 20]. For a total irradiation of the rabbits in doses of 500-100 rad, the excitability of the analyzer increases during the first hours after the effect. For a dose of 500 rad and more, there is suppression of the reflex activity as well as inhibition of the vestibulo-somatic and vestibulo-vegetative reflexes.

PERMISSIBLE LEVELS OF IRRADIATION

A necessary link in the chain for guaranteeing the radiation safety of space flights is a determination of the permissible levels for the effect of cosmic radiations during the flight. A clear, scientifically based regulation of the permissible levels for irradiation predetermines the nature of the answer to many questions on this problem.

It is well known that, for those people working with internal and external sources of ionizing radiation (researchers in the USSR, USA, and other countries), the maximum permissible levels of irradiation have been established as equal to 0.1 rem per week, i.e., 5.0 rem per year. The existing norms of irradiation are /472
maintained, as a rule, by industrial technology, by adequate protective devices, by the possibility for a worker to turn to other effects which are not related with the effect of radiation in the case of overexposure, etc.

However, considering the particular physical features of cosmic radiation (composition, intensity, spectral energy characteristic), the calculated data show that prolonged space flights (to Mars, Venus, and other planets) are necessarily linked with the effect on astronauts of ionizing radiations in doses which which greatly exceed 5.0 rem per year. Thus, the existing norms which are accepted when working with sources of penetrating radiation under terrestrial conditions are not applicable to space flights. Therefore, we need special new approaches to the problem of establishing the permissible levels of irradiation of the crew in the craft, in relation to prolonged space flights.

The conditions guaranteeing radiation safety of space flights, in our opinion, require that the doses of ionizing radiation be divided into three groups: permissible doses (PD); doses of warranted risk (DWR); critical doses (CD).

A permissible dose is a dose of ionizing radiation, an exposure to which does not cause any significant somatic injury to a human being (in the light of contemporary data) throughout his entire life. Such doses can be recommended as the norms for brief space flights, and an excess of these doses should be eliminated by devising physical protection and be selecting special orbits.

A dose of warranted risk is a dose of ionizing radiation, an exposure to which (in the light of contemporary data) causes only isolated cases of weak clinical symptoms of radiation damage. These doses can be recommended for prolonged space flights when the biologically active dose is accumulated mainly as a result of galactic cosmic radiation.

A critical dose is that dose of ionizing radiation, an exposure to which (in the light of contemporary data) can lead to clear clinical symptoms of radiation damage. This dose, when received by an astronaut in an accidental situation, should be a signal for therapeutic, prophylactic, and medical intervention.

In our opinion, such a classification of the doses is extremely necessary, considering the varying nature, tasks, and length of space flights.

One of the next steps in the conquest of outer space, obviously, is a manned flight to the Moon. This flight, from the point of /473
view of a physical and radiobiological evaluation of the radiation danger, is much more complex than the previous orbital flights of the craft "Vostok" and "Voskhod", and therefore requires special examination.

According to calculated data, a flight to the Moon and back to the Earth should not last more than 10-15 days [3]. In this case, the crew of the spacecraft would be affected by galactic cosmic radiation, radiation from the radiation belts of the Earth, and

possibly radiation from solar flares, if the latter should occur during the flight.

Having evaluated the radiation danger, we deem it necessary first of all to formulate the following positions which must be considered in finding recommendations for the permissible doses in relation to a flight to the Moon.

First of all, the physical parameters of the GCR and the radiation of the solar flares are such that it is not realistic to try to produce a protection which would almost completely absorb the ionizing radiation; even theory, in general, can show this. The astronaut will be exposed to doses which will exceed the natural level of radiation which affects human beings on Earth. In relation to this, regardless of whether or not the biological effect of the ionizing radiation is critical, the summary dose during the flight to the Moon (even if only because of the GCR) will be biologically active. Because of this, in designing radiation protection, it is important that we make a rational approach to an organization of the entire system of radiation safety, considering the actual technical possibilities for guaranteeing flight safety. Naturally, having evaluated the radiation danger of the flight to the Moon, and having admitted a definite tenable rish, we must consider the existing knowledge on the biological effect of ionizing radiation and the technical possibilities for guaranteeing the success of the space flight.

Secondly, we think it valid to assume that under the conditions of a space flight to the Moon (up to 15 days), the possible total irradiation of an astronaut because of the GCR, the radiation belts of the Earth, and the solar flares can be evaluated as a single irradiation.

Thirdly, it is important that the crew which is carrying out the space flight will not be subjected as a rule to additional irradiation related to accomplishing operational obligations.

Fourthly, the uniqueness of the conditions being examined is also determined by the fact that a strictly-limited number of people will be exposed to the irradiation.

Considering the specific features of a brief space flight /474
which we have examined (the irradiation of a limited number of people, the single "occupational" exposure, and the long-term experiments of radiobiologists in evaluating the biological effectiveness of ionizing radiation in relation to human beings and experimental animals), we can assume that a dose of 15 rem is the basic one on which we can work out a system for radiation safety of a space flight to the Moon.

An evaluation of the radiation safety under the conditions of prolonged space flights, and a determination of the tenable

values for the doses which would guarantee the vitality and working capacity of the astronauts, are a complex problem. This complexity is caused by the following circumstances:

(1) There is a very small quantity of data on the Values for the doses and on their distribution in time for the actual conditions of a space flight (most of the published results were obtained by calculations).

(2) We have a very insufficient amount of knowledge on the particular features of the effect of various types of cosmic radiation and their relative biological effectiveness.

(3) There are practically no materials which were obtained by modeling a radiation effect in relation to a prolonged space flight (the chronic effect of radiation for 2-6 years in relation to the single effect of periodically-repeated irradiation).

(4) There is not enough data on the rules for the recovery after radiation damages under the conditions of the repeated effect of ionizing radiation.

(5) There are definite limits to transferring the results obtained in an experiment to the cases of animals or human beings.

Thus, any evaluation of the doses and recommendations regarding this problem will remain tentative. Only by accumulating knowledge and introducing the corresponding corrections will there be a minimum divergence between the preliminary values of the permissible doses and their real values.

In examining the radiation danger and the acceptable doses of ionizing radiation in relation to prolonged space flights (of several years) at this stage of our knowledge of the radiation situation in space and the biological effect of radiation, it is expedient that we speak of doses of warranted risk, since the dose that is absorbed only because of the GCR can greatly exceed 15 rem, the value for the permissible dose which re recommended for shorter-term space flights.

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THE PROBLEM OF DETERMINING THE PERMISSIBLE DOSE OF IONIZING RADIATION FOR THE CREW MEMBERS OF SPACECRAFT†

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ABSTRACT: A number of aspects of the problem of determining the permissible dose of ionizing radiation for the crew of spacecraft are examined in this article.

It is proposed that the following three levels of doses be regulated: the permissible dose (PD), the dose of warranted risk (DWR), and the critical dose (CD). It is shown that the values for these doses should vary for brief space flights and for longer-term and longer-range flights in space.

On the basis of an analysis of the clinical observations, the authors consider that the PD, DWR, and CD for brief space flights are 15, 50, and 125 r, respectively.

It is well known that one of the inevitable factors affecting /476 human beings during a space flight is ionizing radiation. The radiation during a flight comes from three principal sources of radiation: galactic cosmic radiation (GCR), the radiation belts of the Earth, and the radiation which accompanies solar flares.

According to contemporary data, the dose rate of GCR in interplanetary space is 34-35 mrad/day. The dose of radiation from the radiation belts of the Earth, on the basis of the available data [23], can be equal to 3-5 rad for a flight through them, with a shield of 10 g/cm^2. The radiation danger linked with solar flares depends on the cycle of the solar activity and the duration of the flight. The intensity of the corpuscular streams generated by individual solar flares can differ by several orders of magnitude. According to the most recent information [24], for a protection of 10 g/cm^2, the protons of solar flares can produce a mid-tissular dose up to 35 rad.

In the light of these data, during a flight over the course Earth-Moon-Earth lasting 10-15 days [7, 11, 53] with a protection of 10 g/cm^2, the astronauts can be subjected to the effect of cosmic radiation within the limits of doses from 4 to 40 rad, depending on the solar activity. For flights to other planets in the

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Solar System, depending on the length of the flight, the total GCR dose absorbed can also increase. Moreover, under the conditions of a prolonged flight, there is also the possibility that the astronauts will be exposed to corpuscular streams from solar flares which differ greatly in intensity.

Thus, calculations show that the crew of a craft can be affected during space flight, by cosmic radiation in doses which exceed the existing norms for occupational exposure. Moreover, for technological reasons [51], it is impossible to equip a spacecraft with a protection from cosmic radiation which would decrease the dose to the levels regulated by the International Commission on Radiation Protection [41].

Considering the above, and noting that the number of persons who are astronauts by profession is very limited, we consider it /477
expedient to make a special classification of the levels of radiation which can be used in evaluating the radiation danger of brief and prolonged flights.

In our opinion [16], we can specify the following three categories of doses: the permissible dose (PD); the dose of warranted risk (DWR); the critical dose (CD).

We are suggesting that, for brief flights, the effect of the cosmic radiation (due to the GCR, the width of the radiation belts of the Earth, and the solar flares) should be taken conditionally as a single effect, although the irradiation could last several days. In this case, we are intentionally exaggerating the anticipated effect since the recovery processes are more pronounced for a prolonged or fractionated effect. Therefore, this assumption can be considered completely valid, particularly because it is intended for the advantage of the astronaut.

For prolonged flights, the irradiation from the GCR should be taken as chronic, as should the repeated acute effects of the protons from solar flares.

On the basis of the arguments presented above, it is necessary to examine separately the materials on the determination of the permissible doses of ionizing radiation for brief flights and for prolonged ones.

In order to evaluate the permissible doses for brief flights, we can use observations on persons who were subjected to irradiation during accidents and atomic explosions, as well as observations of the reactions of persons who were irradiated for therapeutic purposes.

For brief flights, the principal danger lies in the radiation of solar flares which generate doses on the order of tens of rads beyond the existing protective arrangements. In relation to this,

we deem it necessary (in order to establish the value of the permissible dose) to use materials from clinical observations of a general fractionated irradiation for therapeutic purposes. The /4
value of the data from these studies is that when irradiation is used in clinics, there is the possibility, first of all, for obtaining a preliminary evaluation of the condition of the irradiated subjects; secondly, there is the possibility of making an accurate evaluation of the dose of radiation received, which corresponds (to some degree) to the values of the doses to which an astronaut can be exposed during a solar flare and which may exceed his protection.

We had the possibility of observing 97 people, mostly women, who were subjected to sub-total irradiation, either for prophylactic purposes after a radical operation in connection with a mmary carcinoma in the second or third stages, or in connection with a metastatic process, also primarily of mammary carcinoma [17, 21, 22]. We used this method of irradiation on the basis of a longer experiment using total irradiation in oncological practice [62, 68, 73, and others]. The subjects were 30 to 60 years old; most were 40 to 50. The subjects were mainly in a satisfactory condition before the irradiation, which allowed accomplishing the radiation therapy under ambulatory conditions. All the subjects underwent irradiation by the RUM-3 x-ray apparatus at 180 kV, 15 ma, with a filter of 0.5 mm Cu + 1.0 mm Al, a distance from the source to the center of the body of 120 cm, and a dose rate of 3.6-5.0 r/min. The upper and lower halves of the body were irradiated in turn, from the front and from the back. The irradiation was in a single dose of 25 r every day, or (in some cases) up to total doses of 100-300 r in a day.

The reactions of the subjects to the radiation were determined by considering their general condition and the dynamics of the changes in the peripheral blood. The clinical symptoms of a primary /4
reaction were determined according to the following three degrees of severity:

The first-degree reaction involved symptoms of a general reaction which appeared infrequently and were not very pronounced (a slight weakness, headache, nausea, decrease of appetite, mild vertigo, etc.).

The second-degree reaction involved symptoms which led to a certain decrease of the working capacity (general weakness, persistent nausea, an emetic period, a pronounced decrease of appetite, olfactory and taste distortions, headache, vertigo, etc).

The third-degree reaction involved symptoms which caused a pronounced decrease of the working capacity (intense general weakness, lack of appetite, intense nausea, many emetic periods, apathy, an increase of the body temperature, chills, a pronounced distortion of taste and olfaction, a strong headache, severe vertigo.

THE RATE AND SEVERITY OF THE GENERAL REACTION VERSUS THE DOSE

Dose, r*	Total no. of subjects	Reaction						Degree of Severity of the Clinical Symptoms								
		No Clinical Symptoms			Pronounced			First Deg.			Second Deg.			Third Deg.		
		No. of subjects	%	Confidence Interval	No. of subjects	%	Confidence Interval	No. of subjects	%	Confidence Interval	No. of subjects	%	Confidence Interval	No. of subjects	%	Confidence Interval
25	97	79	86,1	72,6—88,7	18	18,4	11,3—27,4	10	10,2	5,0—19,6	6	6,1	2,6—14,5	2	2,1	0,3—8,0
50	69	47	66,7	55,8—78,6	22	33,3	20,9—43,7	15	21,7	14,0—36,2	6	8,8	4,2—22,7	1	1,4	0,1—10,0
75	66	35	53,1	38,4—63,0	31	49,6	34,3—59,6	26	39,3	30,0—55,9	5	7,7	4,2—26,8	—	—	—
100	61	29	47,6	34,0—59,9	32	52,4	39,1—65,3	22	36,0	29,3—57,7	10	16,3	13,0—42,1	—	—	—
125	42	15	35,7	21,6—52,0	27	64,3	48,0—78,4	18	42,0	36,3—71,9	7	16,6	13,9—54,9	2	4,6	1,5—36,0
150	40	17	42,5	27,0—59,1	23	57,5	40,9—73,0	16	40,0	30,8—66,5	4	10,0	5,4—41,9	3	7,5	3,2—37,0
175	34	17	50,0	32,4—67,6	17	50,0	32,4—67,6	10	29,4	19,4—57,7	5	14,7	7,8—45,3	2	5,9	1,3—33,0
200	32	16	50,0	31,9—68,1	16	50,0	31,9—68,1	12	37,5	24,5—62,8	3	9,4	3,4—39,6	1	3,1	0,1—28,0
225	15	10	66,7		5	33,3		5								
250	10	6	60,0		4	40,0										
300	7	4	57,2		3	42,8										

*The subjects were irradiated in repeated doses of 25 r, as a rule, every day. We considered the total dose as a single irradiation.

The results of the observations considering the degree of severity of the symptoms of the primary reaction, in relation to the value for the dose of radiation, are shown in the table. These data show that most subjects tolerated irradiation in doses of 25 and 50 r very well (81.6 and 66.7%, respectively). With a further increase of the total dose, there was a decrease in the number of people who showed no primary reaction to the irradiation. For a dose of 125 r, only 35.8% of the subjects showed no clinical symptoms of a general reaction.

There was a statistically reliable regularity found in the increase in frequency of reactionary symptoms during irradiation up to a total dose of 125 r, and a subsequent stabilization of the /480
clinical symptoms was found within the range of doses from 125 to 200 r (such a stabilization was probably linked with the possibility of using such values of the total doses for subjects who were resistant to the radiation effect).

For most of the subjects, the primary reaction was not very pronounced, and we evaluated it as a first-degree reaction. The regularity of the increase of the first-and second-degree reaction in relation to the total doses of irradiation was approximately identical, with a maximum at a dose of 100-125 r. The third-degree reaction appeared mainly when the summary dose reached 125 r, with a maximum at a dose of 150 r.

An analysis of the separate symptoms, like an analysis of the reaction on the whole, showed a gradual increase in the frequency of such symptoms as general weakness, loss of appetite, and nausea. A pronounced increase of these symptoms was noted after irradiation with a total dose of 75 r, and the maximum increase was noted within the limits of 125-150 r. We should note that there was an increase in the cases of emesis for the patients after irradiation in total doses of 125-175 r.

We did not observe any clear relationship between the general reaction and changes in the peripheral blood. A maximum decrease in the amount of leukocytes was noted during the periods from the 35th to the 55th days, regardless of the total dose received within the range of 200-400 r and the degree of severity of the general reaction.

However, we should note that there were individual cases when a primary reaction of the second or third degree appeared during irradiation in doses of 25 and 50 r. We observed the appearance of intense general weakness, vertigo, headache, loss of appetite, and intense nausea in 7 subjects (out of 97) after the first irradiation; in three cases, we even observed emesis. For 3 out of these 7 subjects, the appearance of these symptoms served as the reason for terminating the experiment. It is true that for one subject we could never maintain to any degree of reliability that the worsening of the condition was linked solely with the effect of

radiation, since this subject showed pronounced vegetative dystonia before irradiation. According to the clinical indications, we still attempted a repeated irradiation in the other four cases, after various intervals of time (from 1 day to 6 months), and all four subjects again showed a pronounced reaction similar to the reaction to the first irradiation (or more severe). In addition to these 7 cases, 3 other subjects showed a second-degree reaction after the second irradiation (when the total dose of irradiation was 50 r). Thus, in 10 subjects we observed an earlier pronounced primary reaction to the radiation effect in a dose of 25-50 r.

Proof that there was a reaction to irradiation in this group of subjects and not a worsening of the condition related to the original ailment was provided first of all by the fact that within 2-3 days after the termination of the irradiation, all the above-mentioned symptoms disappeared; secondly, the repeated radiation /481
effect again caused the appearance of the same symptoms as were found after the first irradiation. Because of this group, we obtained a certain increase in the frequency of appearance of second- and third-degree reactions for doses of 25 and 50 r. In contrast to this group of subjects with pronounced reaction to the radiation effect, another group of 14 subjects underwent irradiation without any symptoms of a primary reaction, or with only insignificant signs of it. With these subjects, we had the possibility of completing the planned course of irradiation, leading to total doses up to 200-400 r.

Our observations, as well as single cases of an early general reaction in persons described by Miller [67] and Medinger [66] for irradiation by doses on the order of 25-50 r, show the presence in some of them of a very high radiation sensitivity, and they indicate the necessity for a special selection of candidates for space flights. This is also confirmed by the data of experimental studies [10,12]. However, as was noted earlier, we should consider that there is a strict selection of completely healthy people who undergo special training for space flight while under the conditions of the radiological clinic; the people undergo irradiation mainly in connection with malignant neoformations or after considerable operative interventions and various types of therapy, which unquestionably must be reflected in the general condition and the reactivity of the organism.

Thus, having evaluated the frequency and degree of severity of the primary reaction on the shole, we can note that under our conditions of fractionated irradiation, most of the subjects showed either no reaction or an insignificant one (first-degree reaction) for all the dosage levels we imposed. Even for total doses of 125 r and higher, about 80% of the people belonged to this group. Similar data were obtained by Medinger [66].

Other materials for determining the permissible levels of radiation under the conditions of brief space flights can be found

in clinical observations of the reactions of subjects to single general irradiations in large doses (failures of reactors during more or less uniform irradiation, the effect of an atomic explosion, irradiation in large doses for therapeutical purposes). Depending on the intensity of the clinical symptoms and the level of the irradiation doses, we subdivided all the observations into 2 groups.

The first group, according to the classification of G.D. Baysogolov and A.K. Gus'kova [1] referred to thos subjects for whom the value of the irradiation dose did not exceed 250 rem. Such are Cases 6 and 7 of [61], Cases 1 and 2 of [60], Case 5 of [52], the group of people suffering from an atomic explosion at the atoll of Rengeleppa, with a radiation dose of 172 r [54], Case 11 of [64], and another 30 cases in [67].

For the second group of observations, we included those of /482
Soviet researchers [2, 3, 18] as well as Observations Nos. 2, 3, and 4 of Andrews et al. [52] and the observations on the postradiation effects at Hiroshima and Nagasaki [45]. The dose of irradiation for most of the people in this group was within the range of 250-400 rem.

An analysis of the observations of the first group shows that, for irradiation in doses of 100-250 r, most of the subjects show a primary reaction which lasts 1-3 days. In this case, signs of general functional disorders, in combination with slight tissular damage (moderate decrease of the red cells in the bone marrow, lymphopenia, leukopenia, thrombocytopenia), predominate in the primary reaction.

Typical for the second group of subjects was the presence of a pronounced primary reaction which lasted 2-3 days, with features of a clear tissular damage (significant decrease in the number of new medullary cells, pronounced leukopenia, lymphopenia, and thrombocytopenia, with subsequent pronounced clinical signs of radiation sickness.

In evaluating the PD, DWR, and CD of the radiation for brief space flights, we should keep in mind a number of features which do not have to be considered in other situations. In particular, in order to evaluate the radiation danger of space flights, we should consider the possible appearance of a primary reaction to the radiation effect, since the appearance of a second-degree reaction (and, in particular, a third-degree reaction) can entail serious after effects. From the materials we have presented, it follows that with a single irradiation in a dose of 25 r, there are single cases of a primary reaction of the second or third degree; such a dose can not be considered as permissible under the conditions of brief flights. We consider it expedient to set the permissible dose at 15 rem [16]. For such a dose, there are certainly no somatic effects observed [38, 57], while minimum disorders in the form of hematological changes are determined only on the

basis of a statistical analysis of the results obtained for the blood content in a large number of irradiated subjects [57, 71, 72]. A lethal result of irradiation in a dose of 50 r is completely excluded. Considering the above, a dose of 50 rem would be considered by us to be a dose of warranted risk.

The maximum increase in the frequency of primary reactions, on the basis of our studies, (i.e., for fractionated irradiation), is observed for a dose of 125 r (64%). In this case, the number of cases for a second- or third-degree reaction increases up to 21.3%. For the single effect in a dose of 125-175 r [67], 7 out of 12 subjects showed a pronounced primary reaction accompanied by emesis [71]. In comparing our data with the results obtained by Gertsner [58], we can establish that, for a single effect, there is a more intense increase in the frequency of pronounced primary reactions with an increase of the dose than for fractionated irradiation. /483

On the basis of these data, and considering the strict selection and training of the astronauts in preparing for space flight, we can consider 125 r as the critical dose during brief flights [16]. A further increase of the dose could lead to the development of acute radiation sickness, which calls for therapeutic and prophylactic measures.

A much more complicated problem involves determining the norm for prolonged space flights. For the Earth-Mars-Earth run, the duration of the flight is obviously 2.5 to 3 years [5,32]. For this period, the total dose of irradiation due to GCR can be equal to 69-91 rem/year, or 174-274 rem per flight [23,24], while the radiation of solar flares can increase the yearly dose, even with a protection of 25 g/cm^2, roughly up to 550 rem/year [59].

Considering the duration of the flights [2.5-3 years), the radiation effect due to the GCR under these conditions can be calculated as chronic. It follows from this that if in order to determine the doses for brief flight it is necessary to consider the primary reaction to irradiation, then for prolonged flights we should keep in mind the appearance of a radiation effect during more remote periods. Therefore, it is of great importance that we study the materials which involve a prolonged radiation effect under occupational conditions and under experimental ones.

Our own experiment [59], the data of other researchers [3, 25, 39], and an analysis of the many materials summed up by the ICRP, give us the possibility for making a clinical determination of the permissible levels of the effect in relation to prolonged space flights.

For the clinical characteristic of the chronic effect of radiation, we found that the following grouping of observations, in relation to the level for the doses of irradiation, should be made:

Group 1: Those working with reactors [50], accelerators [9, 20, 26, 30], and neutron cores [35, 40], as well as radiologists who began working during the last 3-5 years, and most of thse who use isotopes in science-research institutes. The total values of the irradiation doses, according to calculations as well as measurements, did not exceed 30-50 rem, depending on the stage of the work (6-7 years), and were often equal to 15-30 rem.

On the basis of the clinical characteristics for these people, there were no differences in the data for the control groups [13-15, 42-46, 49]. There were only certain functional changes in /484 separate organs and systems during special clinical physiological studies. These changes did not affect the working capacity, they did not progress, and they even leveled off in the course of prolonged dynamic observation.

Group II: Those who had been working longer (10-15 years), radiologists (during the first years of their work, the maximum value for the occupational radiation stress was 15 rem/year), limited groups of radiographers [42,48], and operators of certain experimental apparatus. These people underwent irradiation which was not uniform in time (they received 2/3 - 4/5 of the total dose of 50-150 r during the first years of work). In this group, we found a more regular vegetative-vascular instability; in some cases, there were clinical symptoms of neurocirculatory dystonia of hypotonic type, and hypofunction of the gastric secretory apparatus. In approaching the upper range of doses, there sometimes developed a chronic radiation sickness of the first degree. These changes occur gradually, and they regress for 2-5 years, when the irradiation is terminated or its level is decreased to the accepted permissible maximum.

Group 3: Mainly radiologists who had worked for 20 years and more, or those who had prepared radium preparations and radium-bearing phosphors. This group represents the smallest number of people. The total values of doses of x-rays or γ-rays are 150-400 r, and even 1000-2000 r [56]. For these people, the intensity of irradiation during different years could exceed the maximum permissible dose by 10-30 times. There is formation of a clinical syndrome of chronic radiation sickness of the first degree and (less often) of the second degree [1,3,19,42]. The periods when clinical symptoms appeared clearly correlate with the intensity of irradiation during certain years (unwarranted violations of the norms and rules for operation). The overwhelming majority of cases in this group involve the appearance of remote after effects from the radiation and isolated harmful results. However, according to out observations, even for the radiologists who had been working for a long time (Group III), for whom the value of the total doses for the most recent years increases insignificantly, there was considerable improvement of the general condition, and the clinical characteristics approached the original data. In this case, we should emphasize that during the terminal observational period,

only in 1% of the cases were there changes in the occupational characteristics [47].

Thus, it follows from the materials presented above that the total value for irradiation doses which did not exceed 100-150 r practically excludes the possibility that a comprehensive syndrome of chronic radiation sickness might arise during the period immediately following (from 1 to 3 years from the moment of irradiation. In the case of the appearance of a radiation syndrome, even /485 in those who were irradiated by rather large total doses (150-400 r), significant reparative-adaptative processes are possible after termination of the effect. According to the opinion of A.K. Gus'kova [19] and B. Rayevskiy [72], the value for a dose of 70-100 r is lower than the level which forewarns of immediate somatic effects. After irradiation in this range of doses, only mild clinical symptoms, which are characteristic of chronic radiation sickness in the most sensitive individuals, are possible.

The experimental data on chronic irradiation of animals are of definite interest in evaluating radiation changes during prolonged space flights, since under experimental conditions we can evaluate the values for the doses of ionizing radiation with greater accuracy and we can follow the biological effects developing in this case with more clarity. From our point of view, particular value must be assigned to those experimental materials in which there are data on the effects which can develop during irradiation of the crew by doses of radiation which correspond to the background of the GCR.

An analysis of the results of a number of researchers, who irradiated mice, rats, and dogs for six months, one year, or two and one-half years in doses of 0.2-0.5 r/day, showed that definite changes develop in the experimental animals during these periods: disorders in hemopoeisis, a change in the quantitative relationships between neutrophils and lymphocytes, and (in a number of cases) leukopenia, thrombocytopenia, etc. [8, 27, 31, 55, 63, 70]; a decrease in the phagocytic activity, the oxygen capacity of the blood, and the catalytic index [27]; a development of disorders in the reproductive system, as reflected by a decrease in the weight index for the testes, a decrease in the number of spermatozoa, and the development of aspermia [27, 55, 70]. In this case, experimental studies which show that a gradual recovery from the disorders in hemopoeisis is possible after termination of irradiation have great significance [8,31]. However, for the animals which underwent chronic irradiation, we can expect an increase in the appearance of tumors and a certain shortening of the life expectancy [65].

A decrease in the dose of radiation by one order of magnitude, under similar conditions for irradiation, either caused less pronounced changes in these processes [28, 31, 33, 37] or else there occurred a more or less pronounced effect of so-called "stimulation". The latter occurred with a certain increase in the relative

quantity of leukocytes, an increase in the number of spermatozoa, and a certain increase in the life-expectancy of the animals [27, 33, 65]. An increase in the daily and total values for the radiation dose by one order of magnitude under similar conditions for irradiation, caused a more immediate development (and a more marked appearance) of these disorders in hemopoeisis, the reproductive system, and other indices [29, 34, 36].

On the basis of the available information on the chronic irradiation of humans as well as animals, it is valid to assume that chronic irradiation up to a total dose of 100 rem/year for 3 years not only does not threaten a fatal result, but also does not cause a substantial breakdown in the working capacity of the crew in the spacecraft during the entire flight. This level of radiation can be considered as the dose of warranted risk for astronauts during the first prolonged space flights. However, considering the possibility of remote after effects and the relatively short period for clinical observations thus far, a dose of 100 rem/year can be considered as only tentative. /486

For an ultimate determination of the values of permissible levels of radiation during flights to Mars and other far-off planets, we need special studies. They should be directed toward making the RBE values of all types of cosmic radiation more precise, studying the remote after effects in the processes of adaptation, compensation, and recovery from the changes in the irradiated organism, and studying the combined effect of ionizing radiation and other factors under the conditions of prolonged space flight.

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THE BASIC PRINCIPLES FOR OPTIMUM SHIELDING OF NUCLEAR APPARATUS ON BOARD SPACECRAFT

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ABSTRACT: Principles for planning protection from nuclear apparatus on board spacecraft are established in this article; the necessity is shown for changing and supplementing the approaches for designing shielding of stationary nuclear reactors. Particular attention is given to the selection of criteria for radiation safety. These criteria are highly important in formulating the problem of optimization of the shield, for the purposes of achieving its minimum possible weight. The principles presented in the article allow for considering the particular features of using reactors on board the spacecraft.

It is well known that future research and conquest of outer space is inseparably connected with nuclear power [1, 16, 19]. In relation to this, in order to guarantee radiation safety during space flights, there should be advance planning [3, 17] for protection from the radiation of nuclear power plants (NPP) and nuclear jet engines (NJE). /489

At the present, a large experiment is being devised for designing a radiation shield for stationary and portable nuclear installations [2, 4-6, 7-12]. This experiment will undoubtedly involve designing a shield for nuclear apparatus aboard spacecraft. However, the rigid weight requirements for a shield aboard a spacecraft force us to find additional possibilities for decreasing the weight of the shield. Therefore, it seems expedient to us to examine in detail the principal questions related to the problem of shielding against nuclear apparatus on board a spacecraft.

Modern methods of designing a shield essentialy lead to a determination of the radiation dose in the protected region, for different variations of the shielding installations and equipment. The variations examined are selected on the basis of results of experimental or simulated tests with the apparatus or with corresponding prototypes, considering the general structure of the nuclear apparatus. By comparing the results of calculations for different variations, the best (i.e., those with minimum weight) are selected.

A substantial disadvantage of these methods is that they do

not provide for determining whether or not the best variation is optimal, or how far it is from being optimal, since in this case only previously-selected variations are compared and an optimum solution may not be found.

Obviously, a successful solution to the problem of shielding against the radiation from nuclear apparatus on board spacecraft /490 depends greatly on the correctness of the problem's formulation.

We are attempting to trace the development of the principal tendencies in planning a low-bulk shield, in order to formulate the problem of optimization of nuclear apparatus on board spacecraft.

FORMULATION OF THE PROBLEM OF OPTIMIZATION OF A SHIELD

In the case of using nuclear power in a spacecraft, we can consider a shield optimal when it has a minimum weight and satisfies the requirements imposed on it. Such requirements could be the criteria for radiation safety, radiation resistance, etc. The weight of the optimal shield depends primarily on the correct selection of these criteria.

According to modern concepts, the basic extent of radiation safety for a human being depends on the dose of radiation obtained during a definite period of occupational irradiation. The value for the maximum permissible dose can change, depending on the designation of the equipment and the contingent of people operating it. These changes are related to the types of radiobiological effects which exist under concrete conditions.

The rated levels of radiation are determined on the basis of the maximum permissible dose as well as the degree of serviceability of various environments, i.e., by determining the regulation of the conditions when a human being is in a zone of dangerous radiation. The fact that in practice the maximum permissible levels limit the maximum values for the dose rate in each type of environment reflects the indefiniteness of the information (applied in designing) on the probability that the subject will be located at each point in this environment, and it guarantees a certain safety factor. It follows from this that the less the likelihood that a human being will be at various points in a zone of dangerous radiation is regulated, the more the shield differs from an optimal one.

In the simplest case, when the permissible levels of radiation are identical in all directions, optimization can be obtained with a stratified distribution of the protective material. Such a simplified formulation of the problem is valid because in comparison with the thickness of the actual shield, the nuclear reactor (as a rule) can be considered as a point isotropic source. In designing shields for nuclear reactors, the levels of radiation are limited at the surface of the shield, in order to guarantee access to the equipment and to satisfy the requirement of radiation safety in areas surrounding the reactor.

The designing of shields for portable nuclear reactors, the operation of which involves a higher degree of regulation, shows the need for a significant differentiation of the planned levels of /491
radiation in the shielded areas [11]. This leads to a non-uniform thickness of the shield in various directions, while the optimization in this case is found in a distribution of the layers of the materials in each of the directions being considered. A rather small difference in the planned maximum permissible levels for various areas, and thus a slight irregularity in the thickness of the shield, requires calculating the dose in each direction independently.

A more complex formulation of the problem is found in the necessity of shielding the cabin of the craft from the radiation of its nuclear power plant [20]. The small dimensions of the shielded region lead to a great irregularity in the thickness of the shield, i.e., a shadow protection. However, the fact that the radiation passes around the shadow shielding because of its scattering in the air necessitates partial shielding of the reactor from the opposite side; this has led to an attempt to rearrange some of the shielding material around the cabin. A strict mathematical determination of the optimal shape of the shield for the reactor and the cabin [20] has shown the necessity for a substantial change in the formulation of the problem, including an increase in the number of variable parameters which describe the shield. The criterion of radiation safety in [20] was the dose at a certain point of the shielded region.

However, it was shown in [13] that the shape of the cabin shield changes substantially in relation to the position of this point, if the dimensions of the cabin are comparable to the distance to the reactor. The source of radiation in [13] and [20] was a point. Therefore, the thickness of the shielding determined its external profile as well. Moreover, the reactor and the shield can be considered as points in examining the range of the radiation in the air.

In order to avoid indefiniteness in the shape of the shield for the cabin relative to the position of the protected area, the distribution of the probability that the crew members would be at various points in the cabin was considered in [18].

The shielding of the reactor on board the spacecraft is characterized by a lack of surrounding scattering medium. In view of this, the radiation strikes the protected region only from the side of the shield[1]. However, this does not mean that a shadow shield

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[1]It is also possible that there would be radiation scattered over various parts of the spacecraft. The contribution of this component depends greatly on the concrete arrangement of the equipment.

should have a thickness which is uniform in all directions, since its cross-sectional dimensions are comparable with the extent to which the primary radiation is weakened in the shield, and the role of the marginal effect is correspondingly great in the formation of the scattered radiation. This becomes all the more valid when we realize that the reactor can never be considered as a point source in terms of the comparability of its dimensions with the dimensions of the cabin, and since the intensity of the radiation at the surface of the reactor is highly non-uniform. From this point of view, an excessively simplified formulation of the problem was accepted in [17]; an optimum relationship was sought for the thickness of the light and heavy components of the shield (in the form of a sphere) against the radiation of the reactor, presented as a point source. /492

In outer space, radiation coming from the shield and directed past the protected range must be considered only in relation to the possible scattering over various structures. In this case, radiation coming from the reactor and directed past the protected region contributes to the dose which is scattered in the shield. In view of this, it is expedient that there be an arrangement of the materials of the shadow shielding for the reactor of a spacecraft such that the emission of primary and scattered radiation is facilitated in the direction past the shielded area. The shield which satisfied such requirements was called a scatterer in [14] and [15]. In these studies, examples of scattering shields were given, but the so-called disintegration shield was given the most consideration.

The scattering properties of a shield could probably be achieved by spreading out its material. In relation to this, we found it very necessary to reject the traditional location of the shield for transport and stationary reactors (i.e., adjacent to the source), which is strictly valid only for a point source and is completely unclear for an extended one, particularly in the case of small dimensions of the shielded area.

It is obvious that a shield of the scattering type must be examined by considering the actual shape of the reactor as an extended source, while the angular distribution of the radiation generated at each point on the surface of the reactor can definitely affect the optimal distribution of the shielding material.

In view of this, the optimization of the shield must be conducted simultaneously with an optimization of the geometry for the reactor and the density of the soruces for divisions in it. However, because of the complexity of such a combined procedure, we can optimize the shield in relation to a source which is represented as a plane equivalent of the reactor. This implies a preliminary examination of the relationship between the characteristics for the plane equivalent and the type of reactor, and their effect on the optimal shape of the shield, which allows (to some degree) for using the particular features of the reactor as a source of radiation.

The distinctive feature of this formulation of the problem is the lack of limits imposed on the spatial distribution of the shielding material.

Obviously, an increase in the number of variable parameters which describe the shield extends the possibilities for decreasing its weight. In the most general case, the optimization is found in volumetric concentrations of various shielding materials throughout the entire space near the source and the shielded area. In this case, it is obvious that there could never be any representative point in the shielded area, and we could never limit the levels of radiations for that area alone, since the process of optimization, /493 necessarily "constricts " the shielding materials to the local area around this point, and the conditions of radiation safety throughout the entire shielded area are not satisfactory. The use of a representative point in the studies mentioned above was validated by constricting the formulation of the problem, due to the desired limits of the area for the location of the shielding materials (adjacent to the source or the cabin, etc.). Such limits guaranteed a relatively uniform dose field and, hence, radiation safety throughout the entire shielded area.

We consider it possible to use as the criterion, the dose which is average for the shielded area, considering the probability that the crew members might be al all points.

It is obvious that such a criterion allows for any non-uniformity of the dose field in the protected area, and it gives additional possibilities for economy of weight, since the number of variable parameters, can include the probability that the astronaut will be at various points in the cabin. This means that we can find a more successful (from the point of view of minimization of weight for the shield) arrangement of the equipment; the time for operation of the latter and the volume taken up by it are known in advance. As we can see, a number of the parameters for the shield are related to the structure of the spacecraft, other systems in it, and to the conditions of the flight; the optimization of the shield against the reactor must then be undertaken in addition to the optimization of various systems and the craft as a whole.

In this case, we are naturally confronted with the problem of comparing the interrelated systems according to a criterion which is general for all these systems. The multiple requirements imposed on various systems involve, on the whole, the requirement that they operate reliably. The criterion of reliability can be considered as a basis for the entire craft as a whole. Therefore, the optimization of each system in the spacecraft is performed with the purpose of guaranteeing the given reliability that the flight be accomplished with a minimum weight of the craft, or with the purpose of guaranteeing maximum reliability for a limited original weight.

From this point of view, the criterion now imposed on the shielding system, in the form of a fixed value for the permissible dose per flight, excludes the possibility of minimizing the weight of the shield during the processes of general optimization of the systems in the craft. Therefore, our problem is to express the criterion for radiation safety which is imposed on the shielding system in terms of its reliability, or more accurately, in terms of the reliability of the "functioning" of the astronaut [21] or the apparatus under the conditions of the radiation effect, the degree of which depends directly on the weight characteristics of the shield. The solution to this problem would allow using the plane dependence of the reliability for the shielding system on the dose of the radiation effect, in the process of general optimization.

Contemporary radiobiology can provide considerable information /494
on the dose-dependence of various types of radiation damage to an organism. However, in order to use this information in the problem of shielding, we must determine the principal quantitative signs of reliability in the functioning of an astronaut, and we must know how the remote radiobiological effects are related to the reliability in the functioning of the astronaut for various values of the dose. Moreover, in using the absorbed dose as a measure of the radiation effect, we must consider its spatial distribution in the body of a human being, together with the radiation-sensitivity of various organs and tissues which are responsible for the radiobiological effects affecting the reliability of the "functioning". We should add that in optimization of the shielding system, which touches upon other systems of the craft, there can be changes in the conditions of the vital activity of the astronaut which affect the relationships between the radiobiological effects and the dose. In relation to this, it is useful to know the relationship between the reliability in "functioning" and the dose under the conditions of a combined effect of disadvantageous factors involved in the concrete conditions of the flight.

Hence, having examined the problem of optimization of the shield as a component of the optimization of the spacecraft as a whole, the physical characteristics of the shield must be examined by considering the reliability of the optimal shield in relations to its weight for different forms of an NPP or NJE on board the spacecraft.

Thus, an analysis of the principal tendencies in designing a shield against motor reactors allows us to draw the following conclusions in relation to the spacecraft:

The optimization of the radiation shielding should precede the determination of the criteria for radiation safety and the selection of the necessary and sufficient number of variable parameters which are combined in the formulation of the problem.

The principal criterion is the total dose per flight; for

optimization, we must consider the possibility of a non-uniform distribution of the dose rate in the shielded area during the flight.

In the most general case, the optimization is found in volumetric concentrations of various shielding materials throughout the entire space near the source and the shielded area.

The optimum distribution of the shielding materials depends on the spatial distribution of the radiation sources, the arrangement of the habitable compartments, and the structure of the craft as a whole; the optimization of the shield should be examined as a component of the optimization of the craft.

If, by optimization of the craft, we mean a guarantee of maximum reliability in its flight at a given weight, then it is necessary to express the criteria for radiation safety in terms of reliability.

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METHODOLOGICAL ARTICLES

CLASSIFICATION OF THE ELECTROENCEPHALOGRAM OF A HEALTHY SUBJECT (IN RELATION TO THE PROBLEMS OF SELECTION IN AVIATION)

V.B. Malkin, N.M. Asyamolova, and A.K. Kochetov

ABSTRACT: On the basis of an analysis of 900 encephalographic curves recorded on young, healthy men (ages from 18 to 23), 5 types of EEG were classified.

The classification was based on recordings made when the eyes were open or shut. In this case, the amplitude character of the EEG, the degree of expressivity, and the qualitative features of the α-rhythm, as well as the intensity of the slow and rapid components of the EEG, were considered.

The significance of the orienting reaction was shown to be one of the most important factors determining the individual features of the EEG.

The classification was intended for use in aviation and space medicine during dynamic observations of pilots and astronauts in the course of their practical activity.

Recently, both here and abroad, the study of the EEG has been /495
expanded into research in aviation and space medicine, military medicine, sports physiology, etc. This method is beginning to be used
to select the astronauts and candidates of aviation schools, as well /496
as for a diagnostic evaluation of the changes in the central nervous system during the process of flight training, exercises of various types in sports, etc.

For a long time, the electroencephalographic method (in terms of its application in the professional practice of military medicine and work studies) was used mainly for determining gross pathological changes in the bioelectric activity which are particularly characteristic of such diseases as epilepsy, trauma, and cerebral tumors. Most authors considered that the possibility of finding latent forms of epilepsy with the aid of this method was not sufficient reason for a more wide-spread use of electroencephalography for professional purposes.

Recently, certain researchers have shown the possibility of a significant expansion in the use of this method, since it is sufficiently sensitive to reveal certain forms of functional disorders in the central nervous system which are not related to general pathology. Certain authors have shown that the encephalographic method allows finding (in a number of cases) not only neurotic con-

ditions, but also a definite correlation between the EEG and the capacity for flight training or for various types of intellectual activity.

The normal bioelectric activity of the brain was described by studies of the EEG in practically healthy subjects. In this case, despite the obvious descrepancy in the types of pictures of the bioelectric activity, all the authors noted the necessity of dividing the background EEG of a healthy subject into certain types.

Certain authors took the degree of intensity in the α-rhythm as the basis for the classification [12]; others considered mainly the amplitude character [1]. Gastaut [16] described three types of EEG by relating them to the behavior of the subject. The classification proposed by Cohn reflects the degree of the changes in the electric activity of the brain, mainly in terms of changes in the amplitude [10]. Zhirmunskaya's classification included normal types of EEG as well as types of pathologically altered EEG's [3]. There have also been other attempts to classify the EEG's of healthy subjects in terms of constitutional and psychological features [21].

An attempt to use the existing classifications for evaluating individual types of EEG's examined during the process of selection of aviation candidates, during pressure-chamber experiments, during a study of the resistance to the effect of radical accelerations, etc., was found to be ineffective.

In relation to this, there arose the necessity for working out a classification of the EEG which could be used for selection of a special crew, trainees, and flight candidates, during the process of flight activity, etc.

We made recordings of electroencephalograms on more than 900 men, during the process of examining aviational candidates, and during an examination of persons who had been investigated in a hospital and recognized as fit for flight activity. In this case, we made periodic recordings of the EEG on more than 100 men for a duration of 1 to 3 years; in individual cases, we recorded the EEG continuously, day and night (every 3-4 hours for 30 days). /497

An analysis of the materials permitted us to attempt to classify the EEG's of practically healthy men aged from 18 to 23.

METHODS

The EEG recordings were made with the aid of ink-writing encephalographs made by the firms "Alvar" and "Sanei", and on an electroencephalograph made by the "Biofizpribor" plant in Leningrad. The recordings were made under strictly-maintained and identical conditions, with an identical value for the constant time and the frequency band, with standard values for amplification, and a rel-

atively constant interelectrode resistance (3000-10,000 Ω). The amplification of the potentials was such that a calibration signal of 100 μV caused deflection of the pen by 1 cm. In those cases when the average value of the bioelectric potentials was less than 30 μV, the amplification was increased by a factor of 2. The relatively small amplification of 100 μV at 1 cm was used in view of the fact that we used hyposia and hyperventilation tests, which lead to a significant increase of the amplitude of the bioelectric potentials. We used the frontal-occipital leads from the right and left hemispheres. The bioelectric potentials were detected simultaneously by monopolar recording, from the occiput, temple, and frontal region. The principal lead used for our classification was the bipolar frontal-occipital one. We used it as a surveying lead which gave sufficient information on the character of the bioelectric activity.

This lead was selected in view of its high sensitivity to such functional tests as hyperventilation and hypoxic hypoxia. In a comparative evaluation, it was shown that in recordings made under a condition of relative rest, it resembled a monopolar occipital lead: the recordings clearly show an α-rhythm whose amplitude and shape is (in most cases) practically the same as for a monopolar occipital lead. At the same time, for such effects as an oxygen deficiency or hypocapnia, the first changes (appearance of slow waves with increased amplitude, and other symptoms which are characteristic of these conditions) were recorded by the frontal lead. The frontal electrode, which can be considered as passive, to a certain degree when at rest, becomes active under these conditions, while the changes arising in the monopolar frontal leads also appear clearly in the recordings made with the bipolar method. /498

The EEG recordings for the subjects in our experiments were made under conditions of relative rest, and they differed greatly from those used in clinical practice. During the EEG recordings, the subjects sat in a normal room or pressure chamber with diffused or artificial illumination. During the examinations, the subject opened and shut his eyes at the command of the experimenter.

The departure from the traditional rules for EEG recordings was caused by the fact that during the subsequent experiments they were made under such conditions of real activity for the subject that the possibility of EEG recordings according to the generally-accepted methods was excluded.

For the criteria for classification of the EEG's, we used the recordings made when the subject's eyes were open or shut. In this case, the changes in the EEG which occurred during the change in the recording conditions (shutting of the eyes) were used as one of the indices which characterized a normal EEG.

We took as a basis, a visual analysis of the EEG which was made by several people (independent of one another) for the purposes

of a more objective evaluation. In addition to this, we made a histographic analysis of the EEG for more than 100 subjects and this data was used for making the quantitative characteristics more accurate: the degree of intensity of separate rhythms and the level of the total bio-electric activity.

Particular attention was given to the α-rhythm, its duration and amplitude, the regularity and shape of the α-waves, and the dynamics of its appearance and disappearance when the eyes were opened and shut. For one of the indices of a change in the α-rhythm, we used the coefficient which reflects the ratio between the α-index when the eyes were shut and the α-index during the EEG recording when the eyes were open. Moreover, we considered the degree of intensity of other rhythms in the EEG. In a number of cases, in order to evaluate certain changes, we used the correlation between the nature of the bioelectric activity for the brain activity and the frequency of heart contractions.

Of particular importance for us, in our approach to the study of a classification of the EEG's, was the fact that an analysis of our studies (continued for many years) showed the following: for each subject, there is a rather structly maintained individual type of EEG. In relation to this, we treated the EEG as a very important element of the individual physiological portrait of a human being. We are of the opinion that only on the basis of scientifically based theory for the evaluation of the individual portrait of a human being, and with a formation of generalized type-portraits, can we conduct successful examinations to determine the degree of the changes caused by various effects and certain functional tests.

RESULTS /499

A recording of the bioelectric activity of the brain (the EEG), as we already mentioned, has a strict individual picture. This is particularly noticeable even during a visual evaluation of the curves recorded for subjects under identical conditions for 1 to 3 years.

On the basis of an analysis of the EEG, we find it expedient to define five principal types of EEG.

The first type was the most wide-spread, found in 72% of the subjects; it is characterized, in the recordings made when the subject's eyes were shut, by a regular, clearly-pronounced, α-rhythm. The amplitude of the α-rhythm in most of the cases varied from 50 to 100 μV; in individual subjects, it reached 140-150 μV. The α-index was greater than 50%, i.e., in the EEG for closed eyes the α-rhythm took up more than half of the recording in time. The β-rhythm, which alternated with or was superimposed on the α-waves, was 20-25% (β-index). Moreover, certain curves showed a slow activity which took up 5 to 10%. This appeared mainly in single waves

which were clearly expressed primarily at the frontal leads (Fig.1).

In analyzing the recordings made for the subjects when their eyes were open, this type of EEF could be divided schematically into three subgroups. The curves showing a predominance of the β-rhythm, against the background of which there were small groups of α-waves and single θ-waves, belonged to the first subgroup, which made up 64%. In this case, the amplitude of the bioelectric potentials did not exceed 20-30 μV.

In a small number of curves (3.8%, second subgroup), the α- and β-activity was distributed almost uniformly. The particular feature of these curves was that the slow activity in them was fairly well pronounced, so that the θ-index was approximately 20-30%.

Finally, in the third subgroup the principal rhythm was the α-rhythm, which made up approximately 50-60%, and alternated with groups of high-frequency oscillations and single θ-waves. This subgroup was small, and made up 4.2% in all.

The varying degree of intensity for the α-rhythm during the EEG recordings when the eyes were opened had substantial significance for the value of the coefficient which showed the ratio between the α-rhythm for the recordings when the eyes were shut and for the recordings when the eyes were open. In 64% of the subjects who had their eyes open during the recording, the α-rhythm was almost not expressed al all and this coefficient was very high, while in the subjects who had their eyes open, and for whom the α-rhythm in the recordings was clear (4.2%), the coefficient was relatively small and close to one unit.

The second type of EEG includes those curves whose characteristic feature was that the α-rhythm lasted a relatively short time when the eyes were shut, from 1 to 7 sec., i.e., it rapidly disappeared, after which the EEG recording was characterized by an undistinguished, low-amplitude activity (with an amplitude up to 20-30 mV).

In this case, "flashes" of an α-rhythm of higher amplitude (on the order of 40 mV) and up to 80 mV in individual curves, are repeated each time directly after the eyes are closed. They have a roughly identical duration. This particular feature of the EEG is preserved in the same subject rather constantly during various observations, and is found in only 1% of the cases. The recordings made when the eyes were open were characterized by a sluggish, polymorphous activity of a very low amplitude, up to 10-20 mV. When the eyes were shut the coefficient was greater than 1, but relatively small (Fig. 2).

The third type made up 8% of the EEG's. The recordings with eyes shut showed a polymorphous activity. When the eyes were

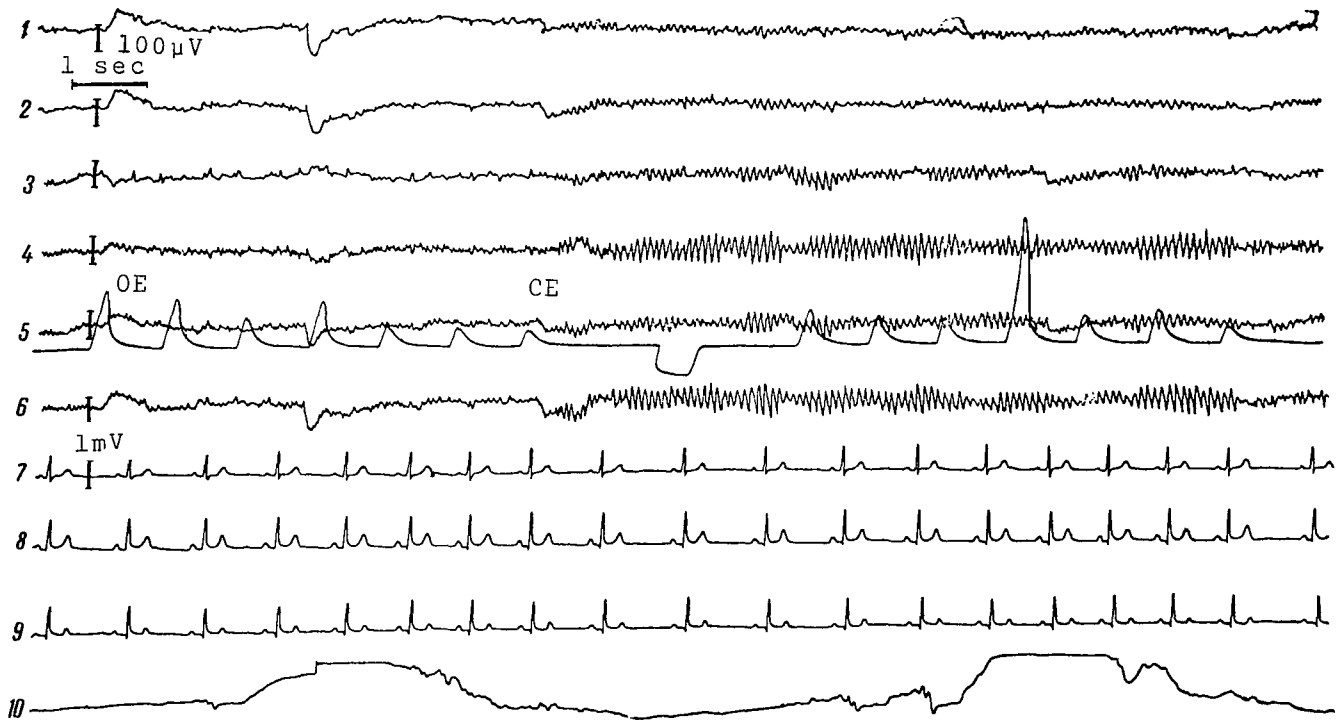

Fig. 1. First Type of EEG, Recordings with Eyes Open and Closed (OE and CE). (1) Monopolar Frontal Lead from the Left; (2) Same, from the Right; (3) Monopolar Occipital Lead from the Left; (4) Same, from the Right; (5) Bipolar Frontal-Occipital Lead from the Left; (6) Same, from the Right; (7), (8), and (9) Ist, IInd, and IIIrd Standard Leads of the ECG; (10) Recording of the Respirational Movements.

opened, the α-waves had an irregular shape and were non-uniform in frequency and amplitude; the β-waves either were superimposed over slower waves, or they appeared in independent short groups. The slow rhythms made up a significant percentage of the recording, and they were represented by waves of varying frequencies (2-8 Hz) and varying amplitude (from 20 to 40 μV). As a response to the closing of the eyes, there were long groups of high-amplitude α-waves, of 60-100 μV, in the frontal-occipital and occipital monopolar leads. Among the α-waves which were non-uniform in shape and varying in frequency, there were diffuse, slower oscillations on the order of 4-8 Hz, with an amplitude up to 120 μV. /501

The fourth type combined the EEG's which we called "with decreased voltage". Sixteen percent were of this type. On closing the eyes, the α-rhythm in the EEG was represented in the form of short groups "with crosspieces" of β-oscillations and with single θ-waves. The amplitude of the bioelectric potentials did not exceed 40 μV, and it was most frequently 25-30 μV. The waves on the EEG which were recorded when the eyes were open had a low amplitude [on the average, equal to 10-15 μV (Fig. 3)].

The fifth type of EEG was characterized by a very low amplitude for the bioelectric potentials, up to 20 μV, and a lack of α-activity. It is difficult to analyze these curves in relation to a determination of the dominant rhythm. We called them "flat". In this case, there appeared groups of α-waves of low amplitude (up to 30 mV) in certain EEG's during repeated recordings with open and closed eyes, after the eyes were shut. Sometimes such an appearance of α-waves could be brought about only by hyperventilation. It is interesting to note that, for many of the subjects with such a reaction, there was s simultaneous high rate of the pulse (up to 90-130 beats/min which is obviously related to emotional stress. Repeated recordings and hyperventilation obviously decreased this emotional stress to some degree and the α-rhythm appeared on the EEG. Therefore, we called these curves "false flat" ones (2%), in contrast to the "real flat" ones which made up 1% and showed (in recordings both with open and closed eyes) a low-amplitude, polymorphous activity (up to 20 μV), a definite predominance of the β-rhythm, and a lack of α-waves at all the leads.

In these subjects, we could not find an α-rhythm, either after hyperventilation or during multiple repeated prolonged recordings; tachycardia was also not found for them (Fig. 4).

DISCUSSION

It might have been appropriate to assume that the departure from the traditional methods for EEG recording should definitely affect the picture of the bioelectric activity in the brain. In this case, we found that when the subject was in an illuminated room and maintained an active position, the lack of strict sound isolation should have led to a certain desynchronization, i.e.,

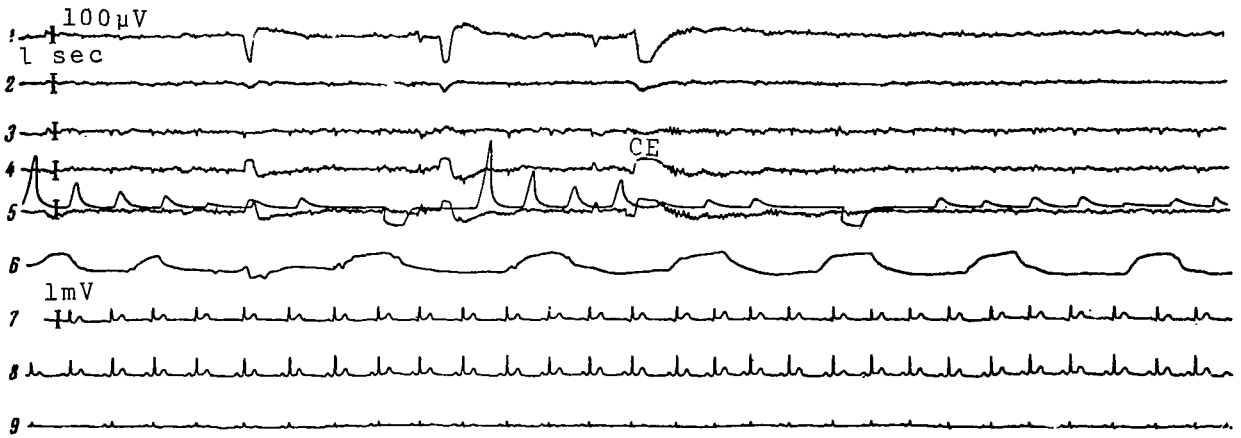

Fig. 2. Second Type of EEG, Recordings with Open and Closed Eyes (OE and CE). (1) Monopolar Frontal Lead from the Left; (2) Same, Temporal Lead from the Left; (3) Same, Occipital Lead from the Left; (4) Bipolar Frontal-Occipital Lead from the Left; (5) Same, from the Right; (6) Respiration; (7), (8), (9) Ist, IInd, and IIIrd Standard ECG leads.

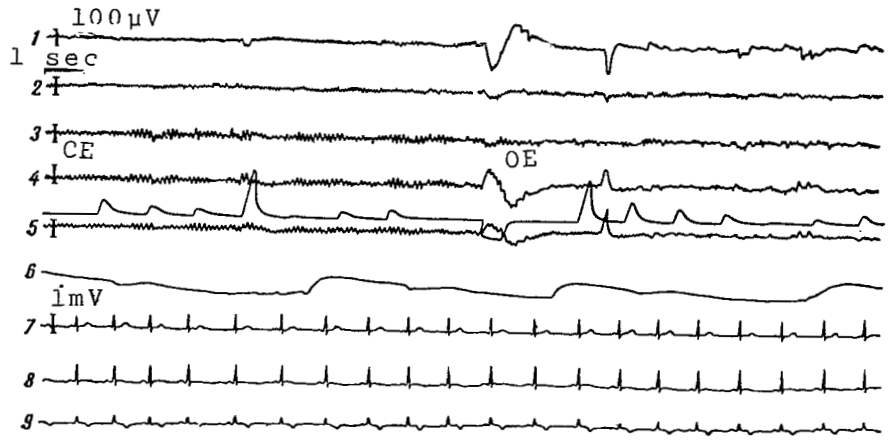

Fig. 3. Fourth Type of EEG, Recording with Closed and Open Eyes (CE and OE). (1) Monopolar Frontal Lead from the Left; (2) Same, Temporal Lead from the Left; (3) Same, Occipital Lead from the Left; (4) Bipolar Frontal-Occipital Lead from the Left; (5) Same, from the Right; (6) Respiration; (7), (8), (9) Ist, IInd, and IIIrd Standard ECG Leads. /503

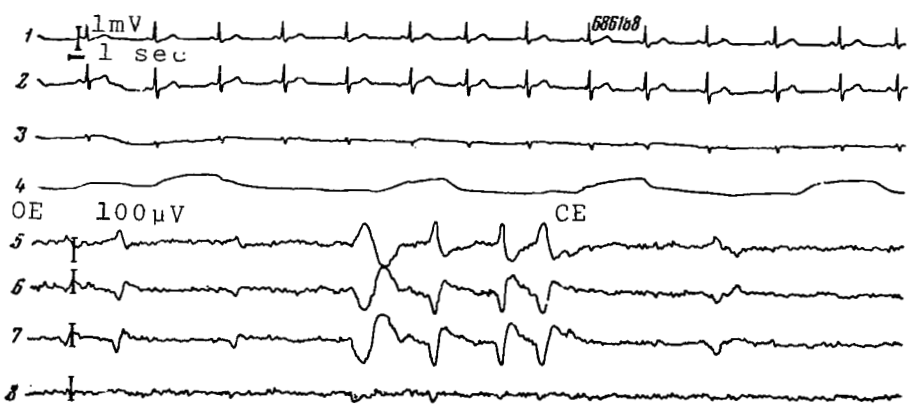

Fig. 4. Fifth Type of EEG, Recordings with Open and Closed Eyes (OE and CE). (1),(2),(3) Ist, IInd, and IIIrd Standard ECG Leads; (4) Respiration; (5) Bipolar Frontal-Occipital Lead from the Right; (6) Same, from the Left; (7) Monopolar Frontal Lead from the Left; (8) Same, Occipital Lead from the Left.

suppression of α-waves and an increase in the number of high-frequency oscillations. /504 However, the results of our experiments showed that the EEG's for healthy subjects under such conditions, when their eyes were closed, not only did not have decreased voltage and less pronounced appearance of α-rhythm as described by standard examination methods, but even the amplitude of the α-rhythm (in certain cases) exceeded the values given by many authors [1, 3, 4, 13, 14]. Thus, for example, according to the data of Zhirmunskaya, the maximum amplitude of the α-waves in the norm must not exceed 110-120 μV; in some of our subjects, the amplitude of the α-waves reached 140-150 μV.

It is clear that the picture for the EEG's of various subjects during recordings with open and closed eyes was nonuniform. However, in both cases, it was rather characteristic for the given individual. In relation to this, in evaluating the type of EEG and its individual characteristics, it seemed necessary to use the coefficients which characterize the ratio between the intensity of the α-rhythm when the eyes were closed and that when the eyes were open. These coefficients can be determined in the form of indices. In this case, we used the histographic method, which allowed establishing the ratio of the total intensity of the bioelectric activity for closed and open eyes.

The use of these coefficients is necessary for evaluating the EEG, because they somehow reflect the level of desynchronization under concrete examination conditions.

The problem of adequate conditions for recording the EEG requires special discussion, since the clinical methods of recording produce a definite level of sensory impoverishment which in itself affects the central nervous system and possibly is a factor causing a certain decrease in the amplitude of the bioelectric potential. Therefore, it is not surprising that in the EEG recordings we obtained under the conditions of a maintenance of relative activity for the subject, the amplitude of the α-rhythm was not lower (and, in some cases, was even higher) than in the studies of other /505 authors who observed recordings of the EEG made under clinical conditions.

We find the conditions which we used for recording the EEG's completely permissible, since they allow us to study the dynamics of the changes in the EEG's during various types of labor activity, including flights into space.

A survey of the experiments studying EEG's during hypoxia and hyperventilation shows that EEG's recorded under these conditions provide a rather complete evaluation of the quantitative and qualitative changes occurring during functional tests.

Moreover, in recording the preliminary EEG of the subjects, there was an orienting reaction. In this case, in the recordings

with open and closed eyes, we can obtain information which characterized the functional changes in the central nervous system caused by this reaction and, in particular, its subsidence.

Each classification was related to a necessary misrepresentation and a definite schematization of the process being examined. In view of this, we are also evaluating the classification we proposed, and are assuming that further studies will allow clarifying, supplementing, developmenting, and formulating more accurately the individual types of EEG. The purpose of our study, in addition to classifying the EEG's of healthy subjects, was to find individual functional changes in the EEG which could characterize the particular features of the central nervous system which play an important part in predicting the reactions to a stress-situation during certain types of activity which require greater nervous and emotional strain.

In relation to this, it is still difficult to evaluate each type of EEG. However, it is now possible to relate certain concepts: thus, for example, the subjects with the fifth type of EEG, in whom the β-rhythm predominated, there was no significant α-rhythm when their eyes were closed and a simultaneous high pulse rate was noted, could be evaluated to a great degree as emotionally unstable. This picture of the bioelectric activity of the brain is obviously related to a lack of normal subsidence or the orienting reaction.

We included those EEG's which showed a rapid exhaustion of α-rhythm in the recordings with closed eyes, in a special group. The basis for this was the observations which showed that such a picture was rather constant and typical for a given individual. We consider it necessary to mention this again, because we naturally suspect that a rapid exhaustion of the α-rhythm is possibly related to its depression as a result of some external stimulus. Actually, such a reaction took place at the beginning for approximately 3% of the subjects; it took time to calm the subjects, after which the reaction disappeared. For some subjects, such an EEG was observed at the beginning of a recording which showed a significant increase in the rate of heart contractions, which is obviously related /506
to increased emotional stress. In relation to this, in some cases the pulse was normal at the end of the observation, while the α-rhythm on the EEG became more prolonged and regular. Moreover, we mentioned earlier that a rapid depletion of the α-rhythm for individual subjects was related to the development of fatigue. This was found in particular during prolonged breathing of oxygen under excessive pressure. However, for a small number of subjects, this picture of the EEG was constant. Thus, we can assume that such a type of EEG, which is found in 1% of the cases, can correlate with certain particular features of higher nervous activity in the subjects. An explanation of this problem has great practical significance for a technical evaluation of the data from the EEG during the process of selecting flight crews and astronauts.

Many authors isolate a special type of EEG as that which is irregular in frequency and amplitude in the α-rhythm, and they link this with "immaturity of the nerve structures" [11,18,22]. In his classification, Gastaut placed those subjects who showed an unstable α-rhythm into a separate group, and he showed that such a type of EEG was not related to "Immaturity", but simply characterized certain young people [16]. Picard examined 309 pilots and also isolated a group of 45 men who showed an unstable α-rhythm and a predominance of the θ-rhythm and single Δ-waves ("labile diencephalic") [22]. Attempting to find a relationship between such a picture of the EEG and psychological data, he noted that the EEG with an unstable α-rhythm and pronounced slow activity is characteristic of "emotionally immature" people with poor self-control. These data, naturally, need testing.

Kukolevskaya and Il'ina, in their classification, also put into a special group those EEG's which showed signs of modulation of the α-waves superimposed over slower oscillation of 4-6 sec, with a maximum amplitude higher than 30 μV [4]. They maintained that such a type of EEG is observed in healthy male sportsmen. In our studies, we found such a type of EEG in 8% of the cases; obviously, they still depended on age factors, since they were found primarily in younger subjects. This question is of definite interest, and it requires further examinations which include psychological research methods.

The curves with decreased voltage of the bioelectric potentials, called "low-voltage fast", are found (according to the data of certain authors) in 12% of the cases [9, 22]. In the classification we propose, such EEG's make up 16% of the cases.

Puister, who examined 700 pilots, noted that polymorphous EEG's with decreased voltage are found in 4.6% of the cases, and are recorded in people who are not adapted for flight training [23]. We /507 are not convinced of the correctness of such a categorical statement.

Almost all the researchers isolate the flat EEG's. According to the data of Jung and Meyer-Mickeleit, they are found in 10-12% of healthy people, and in 8% according to the data of Adams [9, 19, 20].

In our studies, we used the term "flat EEG" in order to describe activity in which the amplitude of the bio-electric potentials does not exceed 20 μV. Most such EEG's are characterized by irregular β- and θ-waves. There is no α-rhythm even in the cases of recording when the eyes are closed. However, during a close examination of the curves, we found certain features which allowed us to divide this type of EEG into two subgroups. We called these subgroups "real flat" and "false flat". The first subgroup contains the EEG's which did not change during repeated recordings and during hyperventilation tests. There were very few of them: 1%. It is possible that the small number of "real flat" curves in our studies was related to the fact that we recorded the EEG's only of young

people (18 to 23 years old). According to the data of a number of authors [9], the number of flat EEG's increases with the subject's age, and they are found most frequently in people who are 40 years old (11%). Thus, the remaining 2% are the so-called "false flat" EEG's. This group was also non-uniform. Having conducted repeated recordings on the same subject at short intervals (5-10 min), we noted that an α-rhythm which is clearer (although it remains small in amplitude: 20-30 μV) gradually begins to appear on the EEG. At the same time, there was also noted a normalization of the pulse (the rate of which was increased to some degree during the preliminary recordings) for these subjects. This gave us the bases on which we could assume that, in the given case, the decrease of the voltage and the suppression of the α-rhythm was obviously related to the emotional reactions of the subjects. Therefore, we called these curves "emotional flat" ones. Such a name was given in order to distinguish them from the other group of curves (and they made up the majority) which also referred to "false flat" EEG's, but in which the α-rhythm is suppressed only after hyperventilation.

Therefore, despite a certain uniqueness of these curves, we consider it necessary to relate them to the group of flat curves, since the principal criteria for the characteristics of the types of EEG are common to them: a decreased voltage of the bioelectric potentials and a lack of a predominant frequency.

Many authors have shown that a flat EEG can be observed for a long time after injury to the brain. In this case, they noted in particular the presence of flat EEG's, in subjects who showed no clinical signs of organic injuries in the brain [17].

Kukolevskaya and Il'ina found that the EEG's with inhibited rhythms and decreased amplitude are found rather frequently in boxers (22%), for whom blows on the head were accompanied not only /508
by concussions, but also by hemorrhages in the brain (in a large number of cases). Therefore, it is very necessary to consider anamnesis for subjects with such EEG's, in order to avoid pathological changes in the bioelectric activity.

In conclusion, we should note that in classifying normal EEG's, there are definite difficulties related to the fact that there is a danger of confusing actual types of EEG's with those changes occurring in relation to the development of an orienting reaction during the examination process. Therefore, it seems to us that the first type of EEG, to which most of the curves belong, had to be subdivided into three forms of orienting reaction in the recordings with closed eyes, which also determined the nonuniformity in the recordings made when the eyes were open.

In itself, the nature of the change in the EEG during the development and subsidence of an orienting reaction (from a practical point of view) is of definite interest in characterizing the

the individual features of the EEG, and therefore can be used for making the calssification more accurate (in particular, for isolating individual subgroups).

Our main task was to work out a classification which could be used during the process of selecting and preparing pilots and astronauts, i.e., those whose specialty is related to the periodic effect on them of various stress-factors. Therefore, the use of the orienting reaction for the purpose of classification is very useful since it, in itself, is a model of the stress-situation to some degree.

For a further, more complete discussion of the significance of various types of background bioelectric activity in the brain of practically healthy people, it is necessary to conduct electroencephalographic studies in combination with psychophysiological studies, with a simultaneous use of various functional tests.

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AN AUTOMATIC ANALYSIS OF DATA ON THE FUNCTION OF EXTERNAL RESPIRATION IN A HUMAN BEING

A.M. ZHDANOV AND K.K. SHCHERBAKOV

ABSTRACT: A method for an automatic analysis of the data on the function of external respiration in a human being is examined.

A block-diagram of the algorithm and the results of the automatic analysis of the data on this function, using the M-12 electronic digital computer, are presented. According to the program developed, the output device writes out the numerical values for ten indices of the external respiration after each respiration cycle, and an additional two indices at the end of each minute.

In examining the function of external respiration in a human /509
being, it is often necessary to make an operative evaluation of the condition of the respiratory system. This problem can be solved completely only when the researcher has at his disposal a comples of indices obtained during the experiment. Existing methods and apparatus are used to analyze data obtained in a graphic or visual form. This analysis, as a rule, is laborious and time-consuming; this naturally decreases the effectiveness of the experiment, from the point of view of evaluating the organism's condition and finding a special solution. The necessity for such an evaluation predetermined the direction of the studies on the automation of an analysis of the data on the function of external respiration.

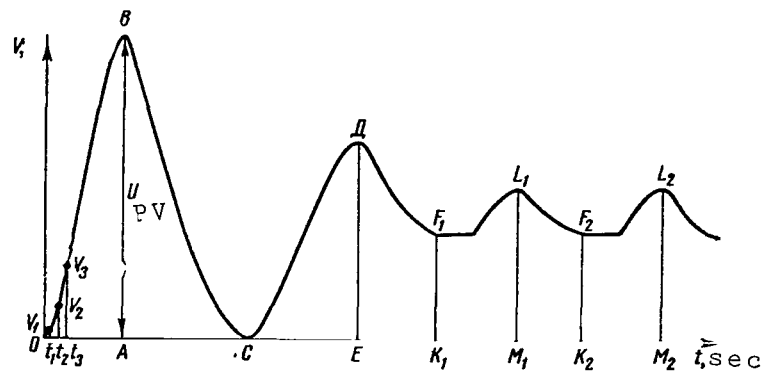
Modern computational techniques provide for automation of the process of analyzing pneumotachometric data, as a result of which /510
we can obtain numerical values for such a complex of indices of external respiration as can allow for conducting both a general regulation of the condition of the respiratory system and smaller, specialized studies.

The system of automatic analysis proposed includes a data unit, a device for studying the function of the external respiration in a subject (DFEX), and a digital computer.

METHODS FOR DETERMINING INDICES OF EXTERNAL RESPIRATION IN A HUMAN BEING

This method for determining the indices of external respiration specifies that the subject must carry out a simple program, so that the first respiratory cycle (inspiration and expiration) occurs at a maximum depth in the forced regime, with a following transition

to respiration at will. In this case, there is an voltage potential (U_V) which alternates in time at the output of the DFEX. The



voltage potential is proportional to the change in the volume of inspired and expired air (V), so that

$$U_V \equiv V;\ V = \varphi(t),$$

where U_V is the output voltage potential of the apparatus, V is the volume of inspired and expired air, and t is the time.

A sample graph for the change in this voltage potential is shown in Fig. 1. An analysis of the graphically-recorded function, $V = \phi(t)$, according to the ordinates at its characteristic points, allows obtaining the quantitative characteristics of the following /511
complex of indices of the external respiration in a human being:

(1) The vital lung capacity (V_{vlc}).
(2) The time for inspiration and expiration (t_{in}, t_{ex}).
(3) The respiratory volumes for inspiration and expiration (V_{in}, V_{ex}).
(4) The maximum volumetric rates for inspiration and expiration ($V_{in,max}$, $V_{ex,max}$).
(5) The reserve volume of inspiration (additional volume) ($V_{r,in}$).
(6) The reserve volume of expiration ($V_{r,ex}$).
(7) The frequency of respiration (F_{res}).
(8) The minute volume of the pulmonary ventilation (V_{pv}).

The determination of the quantitative values for the indices of this complex by a manual analysis of the graph presents certain difficulties related to a development of a significant volume of similar computational materials. The usage of the DFEX-digital computer system in solving this problem allows automating the process of analyzing the original data on the external respiration. The method for determining the indices of the external respiration, based on an analysis of the function $V = \phi(t)$, is presented below.

In order to analyze the data in the digital computer, the graph

for the relationship $V = \phi(t)$ is divided into a number of discrete values for the ordinates ΔV_i, i.e., is quantized at a certain frequency. The frequency of quantization is selected by the following two conditions.

(1) The quantization period must be longer than the maximum time for analyzing the information:

$$\Delta t_{qu} > t_{max.\ anal.}$$

(2) The quantization period must be shorter than any phase of the respiration (inspiration or expiration):

$$\Delta t_{qu} < t_{ph.res}$$

Therefore,

$$t_{ph.res} > \Delta t_{qu} > t_{max,anal} \qquad (1)$$

Considering that with the aid of the DFEX, we can measure the maximum frequency of respiration with F_{res} = 100 breaths/min, we will find the time for respiration for this frequency:

$$(f_{res} = \frac{F_{res}}{100} = 1{,}67\ \text{Hz}), \quad t_{res} = \frac{1}{f_{res}} = 0{,}6\ \text{sec}$$

or the time for one phase of respiration (inspiration or expiration) as 0.6/2 = 0.3 sec, with the allowance that the phases of inspiration and expiration are equal when F_{res} = 100 breaths/min, with no pause in the respiration.

Considering the fact that the speed of response of modern digital computers is thousands and tens of thousands of operations per second, and satisfying the requirement that Δt_{qu} < 0.3 sec, the frequency of quantization is taken as equal to 10 Hz (the quantization period Δt_{qu} = 0.1 sec). In this case, the condition in (1) is satisfied. /512

The values for the ordinates of the volumes with the maximum path (from point 0 to C in Fig. 1) at the points of quantization, expressed in a binary code, are transmitted to a magnetic internal store (MIS). The sequential nature of the differences in the ordinates is determined by the increase in the volumes, which are also sent to the MIS with their signs.

$$\begin{aligned} V_1 - V_0 &= +\Delta V_1, \\ V_2 - V_1 &= +\Delta V_2, \\ &\cdots\cdots\cdots \\ &\cdots\cdots\cdots \\ V_{i+1} - V_i &= \pm \Delta V_{i+1}. \end{aligned}$$

The difference quotient for the volume at the period of quantization determines the value for the volumetric rate at a given point. Strictly speaking, this average value for the rate per quantization period is the following:

$$\frac{\Delta V_1}{\Delta t_{qu}} = \dot{V}_1,$$
$$\frac{\Delta V_2}{\Delta t_{qu}} = \dot{V}_2,$$
$$\cdots\cdots\cdots$$
$$\cdots\cdots\cdots$$
$$\frac{\Delta V_{i+1}}{\Delta t_{qu}} = \pm \dot{V}_{i+1}.$$

The sign in this case indicates the phase of respiration.

The maximum volumetric rates for inspiration and expiration in forced and natural respiration lines are calculated according to the maximum increase in the volume

$$\dot{V}_{max} = K \frac{\Delta V_{max}}{\Delta t_{qu}}, \quad (2)$$

where K is the scale factor.

The time for inspiration t_{in} is determined as the sum of the i-th periods of quantization:

$$t_{in} = \sum_{i=N_b}^{Ne} \Delta t_i, \quad (3)$$

where N_e and N_b are the numbers of quantization periods at the end and beginning of the respiration phase.

In a similar way, we can find the time for expiration t_{ex} and the time for a respirational pause $t_{res,p}$ with (3).

The beginning and the end of a respirational phase are determined by the gradient method according to the following condition: /513

$$\text{grad } F = 0 \quad (4)$$

The current values for the respirational volumes are found as the difference in the ordinates:

$$V_{in,rv_i} = V_{(LM)_i} - V_{(FK)_{i-1}}, \quad (5)$$

while the reserve volumes (supplementary volume) take the following form:

$$V_{\mathrm{r,in}_i} = V_{\mathrm{AB}} - V_{(LM)_i}. \tag{6}$$

The first respirational volume which completes the program at a maximum depth is the vital lung capacity, determined by the following condition:

$$V_{\mathrm{vlc}} = V_{\mathrm{AB}} \tag{7}$$

In calculating the reserve rates for inspiration and expiration, the characteristic points (the maximum rates for the respiration lines) are combined with their corresponding instantaneous values for the respiration volumes.

These values are compared in the MIS with the discrete values for the volumes of the maximum contour. If the values of the volumes coincide precisely with the value posited at the storage unit, then we can find the volumetric rate for this point by the increase of the volume. The difference between the rate obtained and the maximum is also the reserve volumetric rate.

If the instantaneous values for the respiratory volume do not coincide precisely with some of the values in the storage unit, then the difference quotient is found by interpolation. The remaining operations occur in the same way. Then the reserve rate of inspiration (or expiration) is equal to the following:

$$\dot{V}_{\mathrm{r,in(ex),rv}} = \mathrm{K}\frac{\Delta\hat{V}_{\mathrm{mc}} - \Delta V_{\mathrm{rv,max}}}{\Delta t_{\mathrm{qu}}}, \tag{8}$$

where K is the scale factor, and $\hat{V}_{\mathrm{mc}}$ is the difference quotient for the volume of the maximum contour and the corresponding instantaneous value for the respirational volume, for $\Delta V = \pm\Delta V_{\mathrm{rv,max}}$.

The reserve volumes of expiration are found by determining the values of the ordinate $V_{(\mathrm{FK})i}$:

$$V_{\mathrm{r,ex}_i} = V_{(FK)_i}. \tag{9}$$

The current volumes of expiration are characterized by the differences in the ordinates in the following way:

$$V_{\mathrm{ex,rv}_i} = V_{(LM)_i} - V_{(FK)_i}. \tag{10}$$

The minute volume of the pulmonary ventilation is found as the sum of the current volumes of inspiration per 1 min: /514

$$\dot{V}_{pv} = \sum_{i=1}^{n} V_{in_i} + V_{in,supp} \qquad (11)$$

where n is the number of inspirations per minute.

If the end of the current minute falls at an intermediate value for the phase of inspiration, then we calculate the value for the part of the respirational volume $V_{in,supp}$ which is inspired during the time interval of this minute, and we add it to the preceding respiratory time interval of this minute, and we add it to the preceding respiratory volumes (of the given minute).

The frequency of respiration is determined by calculating the number of complete respiratory volumes of inspiration in one minute. The printout of the values for the parameters of the respirational cycle is made at the end of an analysis of each of them. The printout of the values for the pulmonary ventilation and the frequency of respiration is made at the end of each minute.

ALGORITHM OF THE AUTOMATIC ANALYSIS OF THE DATA ON THE FUNCTION OF THE EXTERNAL RESPIRATION IN A HUMAN BEING

In working out an algorithm for the automatic analysis of the data on the function of the external respiration in a human being, the basis on which we posited the method was described earlier.

The solution to the problems, with the aid of the DFEX-digital computer syste, was modeled on the M-20 electronic digital computer.

For the preliminary materials, we used the curve of the function for the volume of inspired and expired air at the time when $V = \phi(t)$, and we punched it on paper tape for a given time. As a result of quantization of the curve, we obtained a number of discrete values for the current volumes (ordinates) which were used as the orignal data for introduction into the digital computer.

The algorithm for the automatic analysis of the data on the function of the external respiration in a human being, whose block diagram is shown in Figure 2, was worked out with a consideration of the fact that the solution to the problem was modeled on an electronic digital computer.

BLOCK 1.

Introduction of the program and the original data.

The punched cards with the program and the original data were fed into the internal storage.

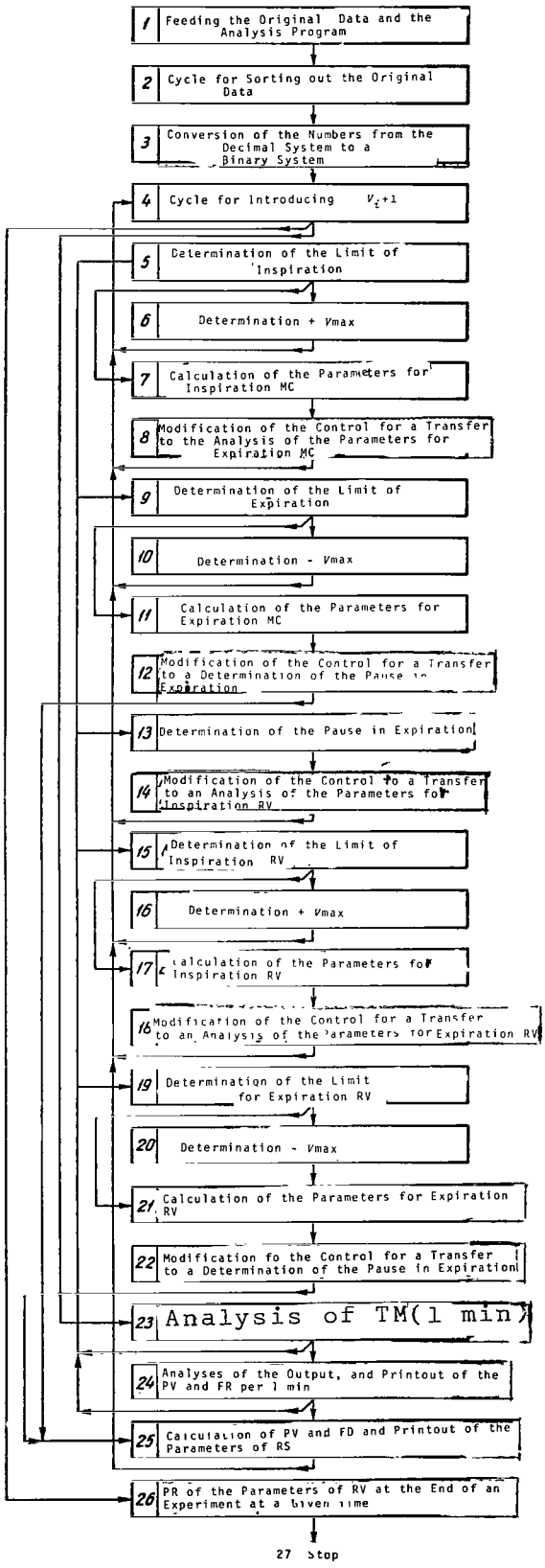


Fig. 2. Block-Diagram of the Algorithm for the Automatic Analysis of the Data on the Function of the External Respiration.

BLOCK 2.

Cycle for sorting out the original data.

In order to save time in feeding the original data and the punched cards for the latter, we perforated according to two numbers. After feeding the original data into each element of the internal storage, we found two numbers. In a given block, the second number was isolated and put into the corresponding storage element, and then the first number was isolated (in the storage element where the two numbers had been, there remained only the first). As a result of completing these actions, a table of the original data is preserved in certain elements of the internal storage (one number in each). /515

BLOCK 3.

Conversion of the numbers from a decimal system to a binary system.

This is done according to the standard program.

BLOCK 4.

Cycle for introducing V_{i+1}.

Before the cycle for introducing $(i+1)$, i-e is sent to the operating element, and after the cycle for introducint $(i+1)$, the values obtained as a result of quantization of the function, $V=\phi(t)$, are sent. At the end of the analysis with $(i+1)$, the value is sent to the operating element, where the i-th value is preserved.

After introducting the value for V_{i+1} into the operating element, there is a transition to an analysis of the time meter. At the end of this cycle, there is a transition to an analysis of the end of the calculation.

BLOCK 5.

Determination of the limit of the Inspiration of Maximum Contour. The limit of the inspiration is determined according to Formula (4).

BLOCK 6.

Determination of the maximum difference $+\Delta V_{max}$ of the maximum contour in an interval of quantization.

The maximum difference $+\Delta V_{max} = \Delta V_i$ for the interval of quantization is determined according to the following condition:

$$\Delta V_{i-1} \leqslant \Delta V_i < \Delta V_{i+1} \tag{12}$$

BLOCK 7.

Calculation of the parameters for the inspiration of maximum countour. (1) The vital lung capacity is determined by finding the respiratory volume at the limit of the inspiration according to the condition in (7). (2) The time for inspiration t_{in} is determined by the programming method for finding the periods. In the internal storage of the digital computer, values are found which were obtained as a result of quantization of the function $V = \phi(t)$. The quantity of the values for V_{i+1} introduced for calculations (BLOCK 4) is calculated with the aid of a programming meter.

The beginning of the introduction of the values for V_{i+1} and the moment of the cessation of inspiration, determined by the presence of the value $V_{in,max}$, are fixed as N_b and N_e, respectively. Since the intervals for quantization are constant, the value for the measured period can be determined according to Formula (3) (3) The maximum rate of inspiration is determined according to Formula (2).

BLOCK 8.

Modification of the control for a transfer to the analysis of the parameters for the expiration of maximum contour.

In this block, the control found in the block for the analysis /516 of the time meter (BLOCK 23) is modified. The modified control provides for a transition to an analysis of the parameters for the expiration of maximum contour.

BLOCK 9.

Determination of the limit of the expiration of maximum contour. This block is accomplished in the same way as BLOCK 5.

BLOCK 10.

Determination of the maximum difference - ΔV_{max} - the maximum contour in an interval of quantization. This block is accomplished in a manner similar to that for BLOCK 6.

BLOCK 11.

Calculation of the parameters for the expiration of maximum contour. (1) The time for expiration t_{ex} is determined according to Formula (3). (2) The maximum rate of expiration V_{exmax} is determined according to Formula (2).

BLOCK 12.

Modification of the control for a transfer to a determination of the pause in the expiration.

This block is accomplished in a way similar to that for BLOCK 8. After completing this block, there is a transition to a calculation of the pulmonary ventilation and the frequency of respiration per minute, and the values for the parameters of the maximum contour are printed out.

BLOCK 13.

Determination of the pause in the expiration.

The beginning and the end of the pause in the expiration are determined according to the condition for determining the end of the expiration (BLOCK 11) and the beginning of the inspiration (BLOCK 7), and also by the following condition:

$$(U_i - U_{i+1}) = \Delta U_i = \text{const.} \tag{13}$$

The value for the pause in the expiration is calculated according to Formula (3).

BLOCK 14.

Modification of the control for a transfer to an analysis of the parameters for the inspiration of the respiratory volume (RV).

This block is accomplished in the same was as BLOCK 9.

BLOCK 15.

Determination of the limit of inspiration of the respiratory volume. This block is accomplished in the same way as BLOCK 5.

BLOCK 16.

Determination of the maximum difference $+\Delta V_{max}$ of the respiratory volume in an interval of quantization. This block is accomplished in a way similar to that for BLOCK 6.

BLOCK 17.

Calculation of the parameters for the inspiration of the respiratory volume. /517

(1) The volume of inspired air $V_{ex,rv}$ is determined by Formula (5).

(2) The time of inspiration $t_{in,rv}$ is determined by Formula (3).

(3) The maximum rate of inspiration $V_{in,rv,max}$ is determined by Formula (2).

(4) The reserve volume of inspired air is determined by Formula (6).

(5) The reserve rate of inspiration $V_{r,in,rv}$ is determined by Formula (8).

BLOCK 18.

Modification of the control for a transfer to an analysis of the parameters for the expiration of the respirational volume.

This block is accomplished in a way similar to BLOCK 9.

BLOCK 19.

Determination of the limit for the expiration of the respiratory volume. This block is accomplished in a way similar to BLOCK 5.

BLOCK 20.

Determination of the maximum difference ΔV_{max} of the respirational volume in an interval of quantization. This block is accomplished in the same way as BLOCK 10.

BLOCK 21.

Calculation of the parameters for the expiration of the RV.
(1) The volume of expired air $V_{ex,rv}$ is determined by Formula (10).
(2) The time of expiration t_{ex} is determined by Formula (3).
(3) The maximum rate of expiration $V_{ex,rv}$ is determined by Formula (2).
(4) The reserve volume of expired air is determined by the condition in (9).
(5) The reserve rate of expiration $V_{r,ex,rv}$ is determined by Formula (8).

BLOCK 22.

Modification of the control for a transfer to a determination of the pause in the expiration. This block is accomplished in the same way as BLOCK 12.

BLOCK 23.

Analysis of the time meter.

The analysis of the time meter is done in the following way. If the number found in the programmed meter N_{pm}, in comparison, is not equal to the given number N_{giv}, then equal to 1 min, there is a transfer of the control to one of the following blocks: 5, 19, 13, 15, 19, (depending on the modification of the control for the transfer to the time meter), i.e.,

$$[(N_{pm}, \psi N_{giv}) \neq 0] \rightarrow (\text{B1 } 5V \text{ B1 } 9V \text{ B1 } 13V \text{ B1 } 15V \text{ B1 } 19) \quad (14)$$

If, in comparing the two numbers, the result is equal to zero, /518 then we must print out the data on the pulmonary ventilation V_{pv} and the frequency of respiration F_{res} per 1 minute, i.e.,

$$[N_{pm}\psi, N_{giv}) = 0] \rightarrow (V_{pv} \wedge F_{res}) \quad (15)$$

BLOCK 24.

Printing out of the pulmonary ventilation and the frequency of respiration. Before printing out the pulmonary ventilation V_{pv} and the frequency of respiration F_{res}, it is necessary to determine the following: at what place in the respirational volume was there a report of 1 min? The accomplishment of this operation provides for the following:
(1) Printing out the pulmonary ventilation and the frequency of respiration, if the report of 1 min. occurred during the inspiration, or,
(2) Ending the analysis of the respirational volume, printing out its parameters, and, after this, printing out the pulmonary ventilation and the frequency of respiration, if the report of 1 min occurred during the espiration or the respirational pause. The place in the respirational volume during the report of 1 min. is noted by the corresponding signs of the time of inspiration Sign t_{in}, of expiration Sign t_{ex}, or of the respirational pause Sign t_{rp}.

In the case when (14) is satisfied and the report of 1 min. occurred during the inspiration, the pulmonary ventilation and the frequency of respiration are printed out, i.e.,

$$\{[N_{pm}\psi N_{giv}) = 0] \wedge \mathrm{Sign}t_{in}\} \to (V_{pv} \wedge F_{res}). \qquad (16)$$

In the case when (14) is satisfied and the report of 1 min does not occur during the inspiration, we note the signs of the time for expiration or the sign of the time of a respirational pause, i.e.,

$$\{[N_{pm}\psi N_{giv}) = 0] \wedge \mathrm{Sign}t_{in}\} \to (\mathrm{Sign}t_{ex} \vee \mathrm{Sign}t_{rp}). \qquad (17)$$

BLOCK 25.

Calculation of the pulmonary ventilation and the frequency of respiration, and thr printing out of the parameters for the respiratory volume.
(1) At the end of the analysis of the maximum contour, there is a calculation of the pulmonary ventilation and the frequency of respiration. The pulmonary ventilation V_{pv} per minute is determined by Formula (11). It follows from Formula (11) that the frequency of respiration per minute is equal to $F_{res} = n$.

Then the values for the parameters of the maximum contour are printed out.
(2) At the end of the analysis of each respiratory volume, there is a calculation of the pulmonary ventilation V_{pv} and the frequency of respiration F_{res}, and the values for the parameters of the respiratory volume are printed out. Then we analyze the condition concerning the presence of signs of a time of expiration or a time of a respirational pause. If one of these signs occur,

then the pulmonary ventilation and the frequency of respiration for the past minute are printed out, i.e.,

$$(\mathrm{Sign}t_{ex} \vee \mathrm{Sign}t_{rp}) \rightarrow (V_{pv} \wedge Fres). \qquad (18)$$

If there are none of these signs, there is a transfer of the control to an analysis of the following respiratory volume.

BLOCK 26. /519

Printing out the parameters of the respirational volume at the end of the experiment, at a given time.

At the end of the experiment, it is determined at what place in the respirational volume there was a report of the given time. For this purpose, we analyze the fulfillment of the conditions in (15) and (16). If the condition in (15) is satisfied, then the electronic digital computer is stopped. If the condition in (16) is satisfied, then there is a calculation of the pulmonary ventilation V_{pv} according to Formula (11) and of the frequency of respiration F_{res} according to Formula (18), and the parameters for the inspiration of the respirational volume are printed out. Then there is an analysis to see if the condition in (19) is satisfied. If this is so, then the pulmonary ventilation and the frequency of respiration are printed out, and the electronic digital computer is stopped. If the condition in (19) is not satisfied, the digital computer is stopped.

RESULTS OF THE EXPERIMENT ON THE AUTOMATIC ANALYSIS OF THE DATA ON THE FUNCTIONS OF THE EXTERNAL RESPIRATION IN A HUMAN BEING

On the basis of the block-diagram for the algorithm developed, we constructed a program for analysis using the electronic digital computer M-20.

In order to evaluate the validity of the algorithm developed, and the possibility of correcting it, we modeled the solution for the automatic analysis of the data on the function of the external respiration.

With the aid of the DFEX device and an ink-writing recorded (using tape), the curve for the change in the volumes of the inspired and expired air during the time $V = \phi(t)$ was written out for a given interval in a definite scale. This curve was quantized manually with the period $\Delta t_{qu} = 0.1$ sec, and the values for the volumes at each point of quantization were determined.

For all the discrete values of the ordinates, we constructed a table of the original data, which were transferred onto punched cards.

According to the algorithm used, we constructed a program for analyzing the original data. For the calculating block, we used

the M-20 universal digital computer. The program, the constants, and the original data were sent, before analysis, from the punched cards to the elements of the magnetic internal store.

The results of the automatic analysis were sent to the writing device. After the end of each respiratory cycle, the numerical values for ten of the volumetric, rate, and time indices of the external respiration were printed out. After each minute of the experiment, there was a supplementary writing of the value for the minute volume of the pulmonary ventilation and the frequency of respiration.

The criterion for the validity of the algorithm used and the program was the coincidence of the complex of numerical values for the external respiration obtained by a manual and automatic analysis of the data. /520

The results of the modeling and an analysis of the data obtained confirmed the validity of the algorithm developed, and provided for determining the technological characteristics of the system for the automatic analysis of the data on the functions of the external respiration and the expenditure of the computing complex.

At the present, the authors are studying a direct introduction of the original data into the digital computer and a determination, in print, of the numerical values for a complex of indices on the external respiration, during the process of experimental and statistical analysis.

CERTAIN PROBLEMS WITH REGARD TO THE USE OF ACCELETRONS (MECHANICALLY CONTROLLED VACUUM TUBES) IN DESIGNING MOVING SYSTEMS, AND THE PROSPECTS OF USING THEM IN MEDICINE

A.V. Yegorov

ABSTRACT: The possibility of using acceletrons (mechanically controlled vacuum tubes) for recording various physiological functions is examined.

An acceletron is a mechanically controlled vacuum or gas-filled tube. The principle of operation of this tube is based on direct /520
control of electric current or electric discharge in a gas by a relative mechanical displacement of the electrodes. This feature distinguishes it from other vacuum or gas-filled devices which are controlled by electric or magnetic fields.

The high sensitivity and reliability of acceletrons, the economy and lack of need for additional amplifying devices and their low weight and bulk allow a considerable increase in the effectiveness and reliability of operating research and experimental apparatus used for experiments or for regulating engine systems.

At the present, acceletrons are still being used very modestly in research apparatus and technology, despite their obvious advantages.

This article is the result of studies intended for finding the possibilities of using acceletrons for recording the following:

Prolonged operational stresses and vibrations acting on an aircraft during flight or on a cabin in a centrifuge;

Shock stresses during catapulting;

Accelerations of various parts of the human body, in studies on the nature of its movements under the conditions of increased gravity or weightlessness;

Certain indices of physiological functions in a human being /521
(ballistocardiograms by acceleration, pulse frequencies, tremors of the hands, etc.).

In the process of carrying out the studies, we compiled (and have now analyzed) sufficient statistical materials on the reliability and stability of repetion for the results of recording the accelerations, with the aid of acceletrons. On the basis of the

studies conducted, we have developed recommendations for further improvements of the design of acceletrons.

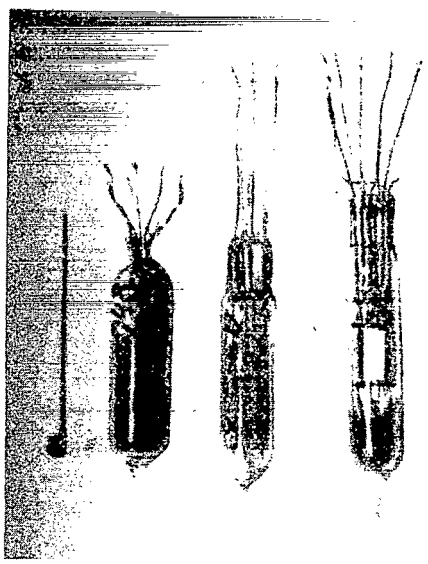


Fig. 1. Interior View of Mechanically Controlled Vacuum Tubes

In the studies, we used acceletrons of longitudinal-control type (AE-3) and sound-control type AE-4. The acceletrons of these types were built to the design of a normal series of vacuum tubes of the "Drop" tupe. The dimensions of the sender units were the following: length, 40 mm; diameter, 8 mm. The maximum weight was 4 g. Interior views of the acceletrons are shown in Figure 1.

Because of the conditions in most of the experiments conducted, we used aircraft-type magnetoelectric oscillographs as recording devices. These oscillographs require significant currents, in order to guarantee sufficient amplitude for "swinging" the loops. Therefore, the studies were conducted with acceletrons of the longitudinal-control type (AE-3).

ACCELETRONS WITH LONGITUDINAL CONTROL (SENDER UNIT WITH CURRENT OUTPUT) /522

The principle of regulation by the electron current of the tube with longitudinal control was based on the change in the intensity of the electric field acting on the electron "cloud" of the cathode, produced by displacing the movable electrode-anode. By using a high-current, fixed indirectly-heated cathode in this acceletron, we could regulate relatively higher anode currents. Figure 2 shows a kinematic scheme of a binary acceletron with longitudinal control.

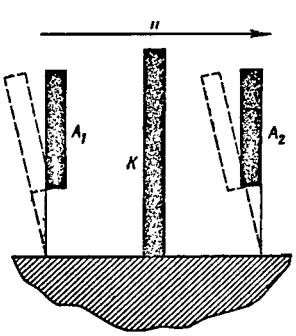


Fig. 2. Kinematic Scheme of an Acceletron with Longitudinal Control. K - Fixed Cathode; A_1, A_2-Movable Anodes.

In this tube, on both sides of the fixed cathode, there are movable anodes with large surfaces. During accelerated movement of the acceletron in the direction of the arrow, the anodes bend because of the inertial mass and assume the position shown by the dashes. Thus, one anode moves closer to the cathode, while the second moves further away.

Using the example of one of the halves of the tube, we can show the relationship between the anode current of the acceletron and the distance between its electrodes (and thus the functional relationship between the current and acceleration).

The distance between the electrodes of the acceletron is much less than their cross-sectional areas, and this permits us to assume that the electric vield in the gap between them is homogeneous [6]. Considering also that the original velocities of the electrons were equal to zero, while the anode and the cathode had equipotential surfaces, and using the following three equations:

(1) The Poisson equation:

$$\frac{\vartheta^2 U}{\vartheta^2 x} = -4\pi\rho, \tag{1}$$

where U is the potential at a distance "x" from the cathode; ρ is the density of the electron "cloud".

(2) The equation for the kinetic energy of the electron,

$$eU = \frac{mv^2}{2}, \tag{2}$$

where e is the charge, m is the mass, and v is the velocity of the electron.

(3) The equation expressing the relationship between the anode current and the density of the space charge, the velocity of the electrons, and the surface of the cathode "S".

$$I_a = -\rho \cdot v \cdot S, \tag{3}$$

/523

As a result of their combined solution, we will obtain the term for the anode current, which has the form:

$$I_a = \frac{k \cdot S \cdot U_a^{3/2}}{L^2} = \frac{C}{L^2}, \tag{4}$$

where $k = 2.34 \cdot 10^{-6}$; S is the active surface of the cathode per square centimeter; U_a is the anode potential in volts; L is the distance between the electrodes in cm; $C = k \cdot S \cdot U_a^{3/2}$.

By examining the Formula (4), we see that the anode current of the tube is inversely proportional to the square of the distance (L) between the anode and the cathode. Thus, in the case of a linear increase in acceleration, the recording will describe a parabolic curve. Using the binary tube in a symmetrical electric bridge, the current relationship for the diagonal line being measured will be subject to an even more complicated law, which takes the following form:

$$I_{\text{diff}} = I_1 - I_2 = 4c\frac{L\cdot\Delta L}{(L^2-\Delta L^2)^2}. \qquad (5)$$

In one series of experiments, we used acceletrons whose structure contained additional correcting springs for the sensing electrodes, according to our recommendations. This allowed the characteristics of the acceletrons to be rectified. Figure 3 shows a graph for a statistical calibration ($\pm$ 1.0q) of a binary tube (Type AE-3) with correcting springs. /524

The operating electrical diagram for connecting the acceletron (Type AE-3) is shown in Figure 4. The normal operating regime of the acceletron is the following: $U_a = U_{cum} << 6.3$V; $I_{a1} = I_{a2}$ = 10mA; I_{act} = 200 mA. The average sensitivity of the tube in terms of the current (in the measuring diagonal line of the electric bridge, compared with the diodes of the acceletron and the balancing potentiometer R_b) was on the order of 0.8-1.1 mA/q, which was completely sufficient for direct operation with Loops IV and V of the K12-21 magnetoelectric oscillograph.

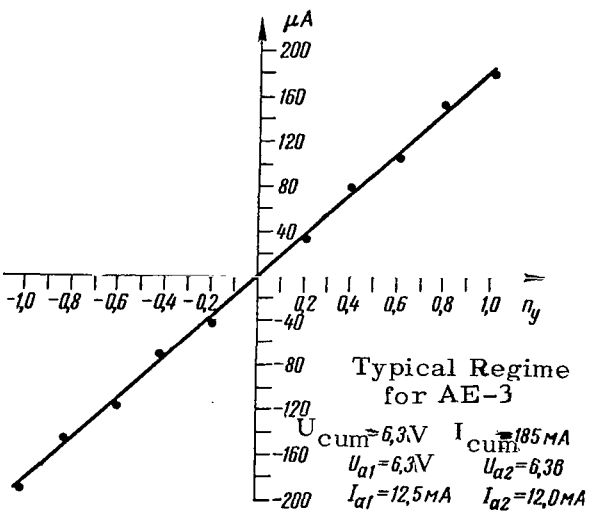


Fig. 3.

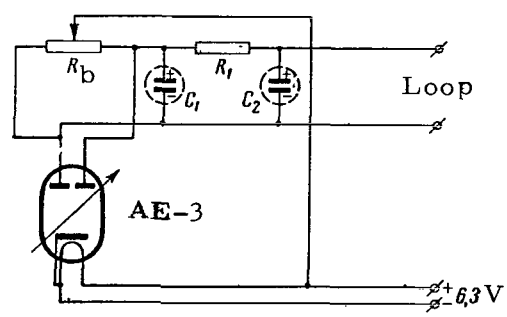


Fig. 4.

Fig. 3. Graph of the Statistical (+1 to -1) Calibration of the Type AE-3 Acceletron.

Fig. 4. Principal Electrical Diagram for Connecting an Acceletron (Type AE-3) to an Electrical Low-Frequency RC-Filter.

It follows from what we have said above that one of the characteristic features of an acceletron of Type AE-3 is its high sensitivity to current at low anode potential. Because of this circumstance, an adequate "supply" for the tube could be obtained from one 6-volt battery with low capacitance. This feature (in addition to the possibility of a direct recording of the accelerations with the aid of the magnetic loops) was most valuable in designing ecomical, reliable, and light research apparatus.

The requirement of particularly economical sender units for accelerations promoted the development of acceletrons with sound control.

SOUND-CONTROL ACCELETRONS (SENDER UNIT WITH VOLTAGE OUTPUT)

In a sound-control acceletron (Type AE-4), there are two electrodes which produce a uniform electric field, in which a thin *U*-shaped oxidized cathode is mounted. This cathode acts as an electric probe.

During the accelerated movement of the acceletron, the loop of the cathode is bent by the effect of inertial forces, so that the distance between the anode and the cathode changes. Thus, the increase in the anode current is proportional to the value of the acceleration being measured. /525

A characteristic feature of this tube is a high sensitivity at a low energy requirement for the power supply. This feature is critical in selecting the type of sender unit for long-lasting, small-size electronic apparatus intended for examining a number of objectives, in which the sender unit for the acceleration should feed directly into the problem-solving and experimental devices.

CERTAIN ASPECTS OF USING ACCELETRONS

An electromechanical tube, just like any other measuring device which has a freely suspended kinematic system, is required to respond without inertia to any changes in the parameter being studied, i.e., the changes in the accelerations acting on the object.

We know that if the angular frequency of natural vibrations in a sensor ω_0 is much greater (by 8-10 times) than the angular frequency of the vibrations in the object ω, the sensor will shift from its relatively zero position by an amplitude proportional to the acceleration of the object, with an error no greater than one tenth of a percent [3]. Thus, the necessary condition for any concrete experiment is to select an accelerometer whose natural frequency satisfies the following condition:

$$\omega \leqslant (0{,}1 \div 0{,}125)\,\omega_0.$$

The natural frequencies of the acceletrons used in the experiments (Type AE-3) were between 150 and 200 Hz; for Type AE-4, they were between 400 and 500 Hz. Thus, with the aid of these tubes, it was possible to measure (with great accuracy) the accelerations acting on an aircraft making complex maneuvers, on an object in the cabin of a rotating centrifuge, on parts of the body of a catapulted subject, on the extremities of a subject carrying out certain movements, etc., i.e., in all cases when the angular velocity of the necessary vibrations in the object did not exceed 15-20 and 40-50 Hz, respectively.

When operating under the conditions of mechanical noise in a system (the vibrations of an aircraft, centrifuge, etc.), whose frequency was commensurate with the natural frequency ω_0 of the acceletron, we used mechanical and electric filters. Correct fastening of the tube to the object can fulfill the functions of the first unit in the mechanical filter, which prevents the effect of a number of mechanical interferences on the acceletron.

The high sensitivity of the acceletrons allowed us to use low- /526
frequency *RC*-filters of *RC* type to combat the mechanical noises on the object. The filtering element of the *RC*-filters is determined by the relationship $R>X_C=1/(\omega C)$, which can vary within a broad range (K = 10-30), depending on the degree of filtration desired.

PROSPECTS FOR USING ACCELETRONS IN MEDICINE

Although research laboratories have made efforts (which are, however, clearly insufficient) to give acceletrons the place which rightfully belongs to them in measurement technology, absolutely nothing is known about them in the medical field, though their technological characteristics could be of considerable importance in the practice of clinical and applied medicine.

In this article, it is interesting to examine (for example) the problem of recording the mechanical vibrations of a human body in response to the force of cardiac contractions (ballistocardiography).

According to the classical theory for measuring aperiodic vibrations, they must be characterized by the accelerations to which the parts of the body being examined are subjected, and by the frequency of the impacts. Thus, in studying the nature and force of the heart contractions, it is not necessary to record the paths or rates of dislocation for parts of the body or for the entire body, as has been done until now both here and aboard; either a single or a double differentiation in time will necessarily lead to perceptible errors, because of the discrete values for the time constants of the differentiating units in the calculating devices. In relation to this, we must acknowledge the completely objective method of studies in ballistocardiography by acceleration (accelecardiography), since the ultimate result of these studies must be

expressed in forces as the functions of the masses and accelerations, i.e., $P = m \cdot a$, and in the nature (nature of the oscillogram) of the pulses of the heart contractions.

The sender unit used in accelecardiography does not have to increase the mass considerably and thus measure the natural frequency of the object being studied (the natural frequency of the human body is approximately 10 Hz). This sender unit, which fulfills all the requirements for a reliable recording in accelecardiography, is a acceletron. Figure 5 shows an accelecardiogram of a human being, recorded from the chest of the subject under the conditions of a climb in a pressure chamber up to a height H = 6000 m; the record was made by the author in optional order. This record has an unusual character, and it cannot be analyzed in the generally accepted order, since it includes qualitatively new objective information on the nechanical activity of the heart, and it calls for a researcher who can enumerate and systematize its components. /527
All that we have said above is also related to the recording of the pulse and of tremors of the hands.

Fig. 5. Accelecardiogram (2) Recorded from the Chest of a Subject, with the Aid of an Acceletron of Type AE-4. (1) Rheogram; (3) Encephalogram; (4) Electrocardiogram; (5) Respiration.

At the present time, a great deal of attention is being given to the problems of human coordination under the conditions of increased gravity or weightlessness. One of the elements of general coordination in man is the nature of the accelerations of the entire human body or the extremities while accomplishing certain

movements. The study of the nature of the accelerations in the movements of a human subject, when conducted with the aid of acceletrons, can completely change the existing,tedious and time-consuming (due to the necessary calculations) methods of cyclography.

For the reasons mentioned above, the sender unit for the accelerations of the human body and the extremities should have the least possible weight and bulk; it should also be accurate and suitable for the task. Such a sender unit is the acceletron.

In one series of esperiments which the researcher conducted, he used his hand (to which the acceletron was fastened) to make certain motions; he then struck a target to mark the end of the motion. Figure 6 shows an oscillogram of the accelerations in the wrist of a human hand, under conditions of weightlessness during a flight in an aircraft along a vertical parabolic curve. /528

The possibilities of using acceletrons in medicine have not been exhausted by these examples. At the present, successful studies are being made of the use of these tubes to record accelerations in such comparatively new branches of physiology as biomechanics.

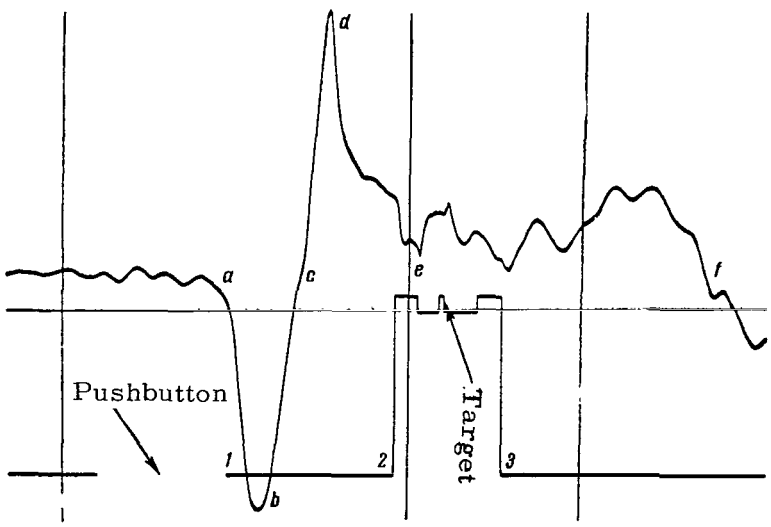


Fig. 6. Oscillogram of Accelerations in the Wrist of a Subject Accomplishing Certain Motions under Conditions of Weightlessness.

The materials presented obviously indicate that acceletrons (accurate, highly-sensitive, small, and economical sender units) can be used successfully in technology and medicine for measuring a wide range of accelerations in mechanical systems, and for regulating programed moving systems.

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